STUDIES IN THE AROMATIC HYDROCARBONS

by

James R. Gorrie, A.H.-W.C.

Thesis presented for the Degree of Doctor of Philosophy.

University of Edinburgh May 1964.

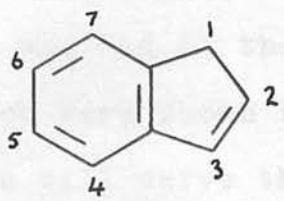
For Helen.

Contents

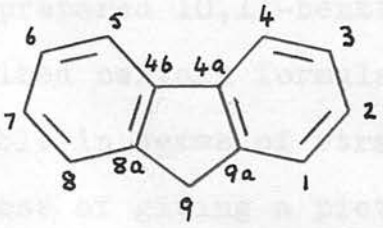
Contents

Nomenclature

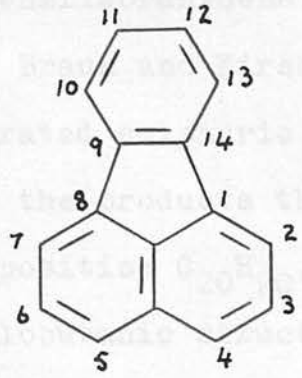
The compounds described in this thesis are numbered as follows:-



Indene



Fluorene



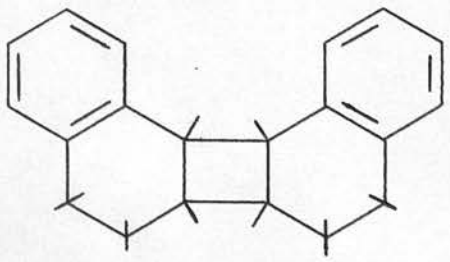
Fluoranthene

INTRODUCTION

The Chemistry of 10,11-Benzfluoranthene

Before dealing with a few of the elegant syntheses of 10,11-benzfluoranthene recorded in the literature today, we must mention the results of earlier research workers, who were later shown to have prepared 10,11-benzfluoranthene, but who had at that time ascribed certain formulations, which were shown to be untenable in terms of strain theory. This will serve the dual purpose of giving a picture of the original work carried out in this field, and introducing the main theme of this study, which is the unambiguous synthesis using classical organic techniques, of an octahydro-10,11-benzfluoranthene.

In 1921, von Braun and Kirschbaum (1) studied the action of concentrated sulphuric acid on 1,2-dihydronaphthalene. One of the products they obtained was a solid (m.p. 93°) of composition $C_{20}H_{20}$, and to this they assigned the following cyclobutanic structure (I).



(I)

Lead oxide dehydrogenation produced a yellow hydrocarbon ($C_{20}H_{12}$, m.p. 165°) to which they gave the name bisnaphthalene i.e., the fully aromatic system corresponding to the above structure.

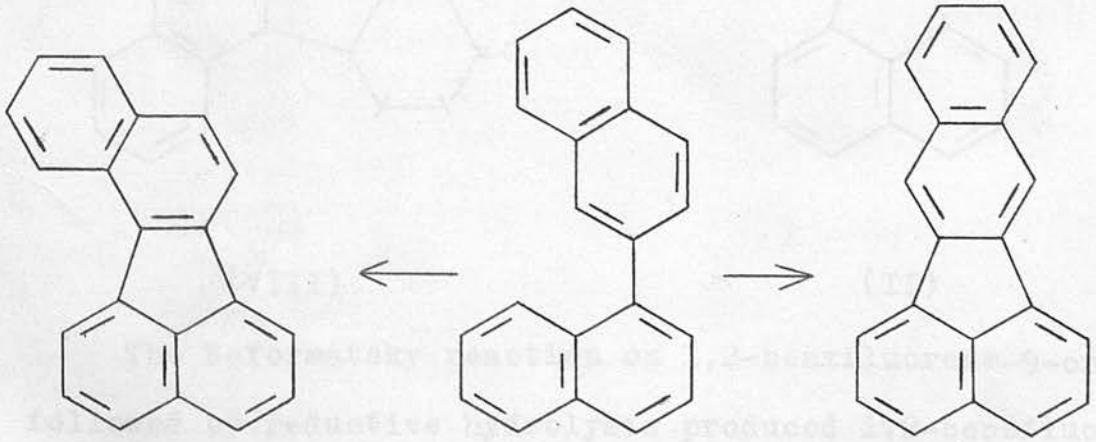
Dansi and Ferri (2) investigated the action of aluminium chloride on tetralin. They obtained a substance ($C_{20}H_{20}$, m.p. 150·5°) which on selenium dehydrogenation gave a yellow hydrocarbon of composition $C_{20}H_{12}$ (m.p. 165°, picrate 195°). Since von Braun's dehydrogenation product, also formed a picrate (m.p. 195°), it was obvious that the dehydrogenation products of Dansi and Ferri and von Braun and Kirschbaum were identical. Summarising this work:-

Author	Intermediate	Reagent	Dimer $C_{20}H_{20}$	Dehydrogenation Product; $C_{20}H_{12}$	Picrate
v.Braun	1,2-Dialin	H_2SO_4	m.p. 93°	m.p. 165°	m.p. 195°
Dansi	Tetralin	$AlCl_3$	m.p.150·5°	m.p. 165°	m.p. 195°

Nenitzescu and Avram (3) and Bell and Hunter (4) considered that the cyclobutane structures postulated by von Braun were incorrect, and suggested that both hydrocarbons of composition $C_{20}H_{20}$ were isomeric octahydro-10,11-benzfluoranthenes. That the dehydrogenation product was indeed 10,11-benzfluoranthene was proved in the following synthetic work.

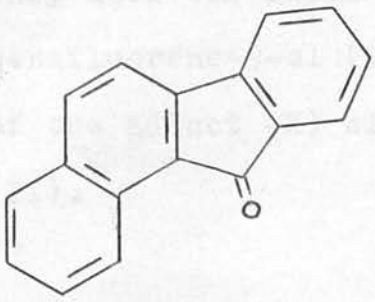
Synthesis of 10,11-Benzfluoranthene

Orchin and Reggel (5) prepared 10,11-benzfluoranthene (II) along with its isomer 11,12-benzfluoranthene (III) by the cyclodehydrogenation of 1,2-dinaphthyl (IV) over chromia-alumina at 500°.

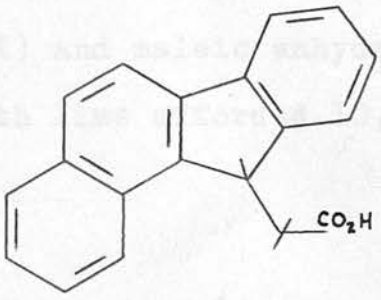


(II) (IV) (III)

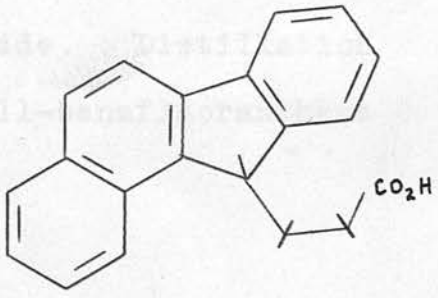
That these authors had originally assigned the reverse structures was pointed out by Moureu et al. (6). Orchin and Reggel (7) later synthesised the two isomers, verifying the observations of Moureu and his co-workers. They developed the following synthesis for the 10,11-isomer.



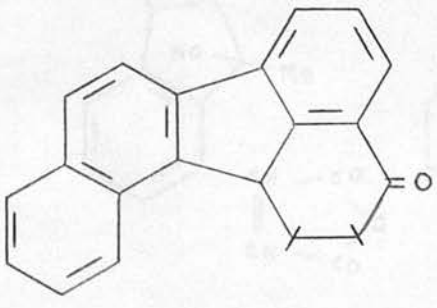
(V)



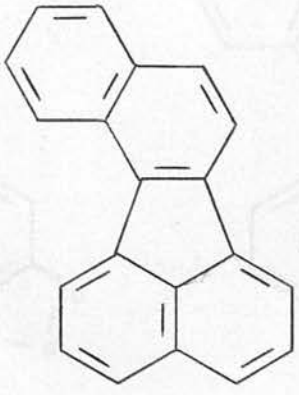
(VI)



(VII)



(VIII)

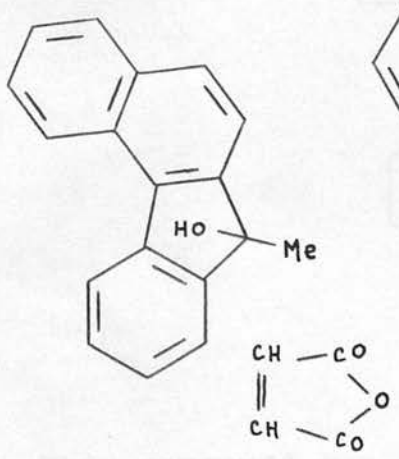


(II)

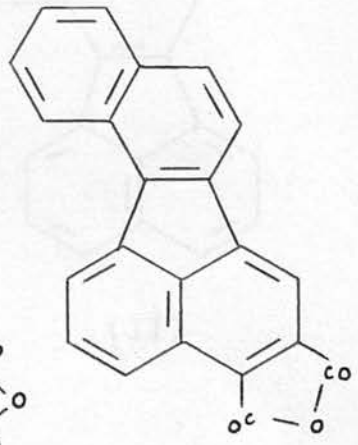
The Reformatsky reaction on 1,2-benzfluorene-9-one (V) followed by reductive hydrolysis produced 1,2-benzfluorene-9-acetic acid (VI). The Arndt-Eistert reaction gave erratic results, and yields of the propionic acid (VII) were generally poor. Cyclisation using an inverse Friedel-Crafts

procedure gave the cyclic ketone (VIII). Clemmensen-Martin reduction followed by dehydrogenation gave 10,11-benzfluoranthene (m.p. 165°) in low yield.

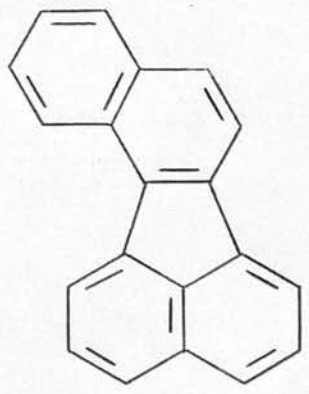
Yet another elegant synthesis of 10,11-benzfluoranthene was that developed by Campbell, Kanna and Marks (8). They used the Diels-Alder reaction between 9-methyl-3,4-benzfluorene-9-ol (IX) and maleic anhydride. Distillation of the adduct (X) with lime afforded 10,11-benzfluoranthene (II).



(IX)



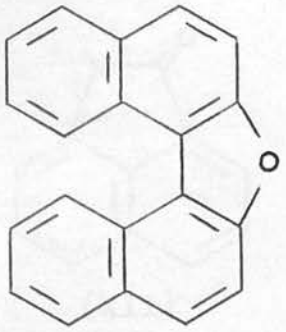
(X)



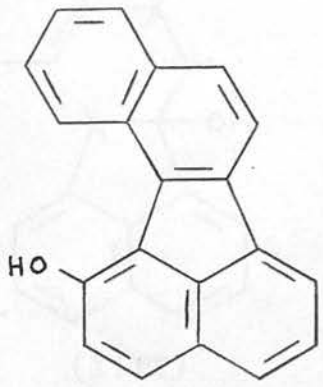
(II)

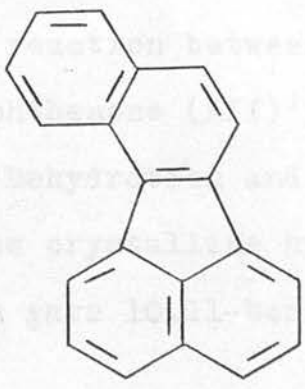
This compound showed the same properties as that isolated by Orchin and Reggel (loc.cit.) and also that claimed to be 10,11-benzfluoranthene prepared by Zinke and Pack (9), by the zinc dust distillation of one of the products obtained from the action of aluminium chloride

on β-dinaphthylene oxide (XI).



(XI)

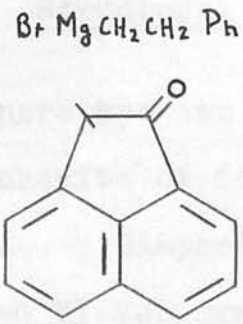




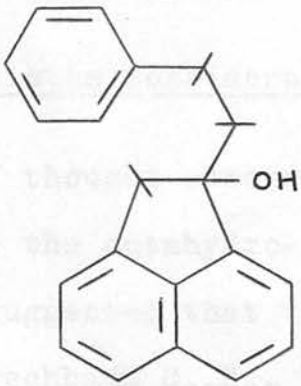
(II)

This compound was also shown to be identical to that prepared by Dansi and Ferri (2), by dehydrogenation of the product from the action of aluminium chloride on tetralin.

Nenitzescu and Avram (3) prepared 10,11-benzfluoranthene by several methods. The following synthesis is interesting:-

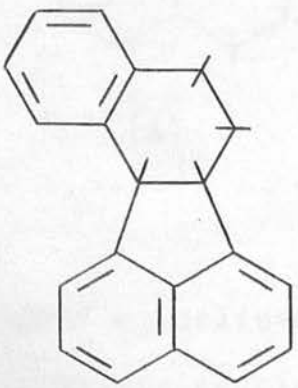


(XII)

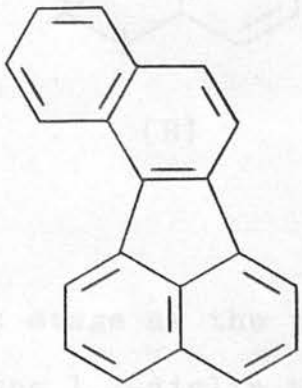


(XIII)

The Grignard reaction between β-phenylethylmagnesium bromide and acenaphthenone (XII) produced the tertiary alcohol (XIII). Dehydration and cyclisation of this gave the colourless crystalline hydrocarbon (XIV) which on dehydrogenation gave 10,11-benzfluoranthene (II).



(XIV)

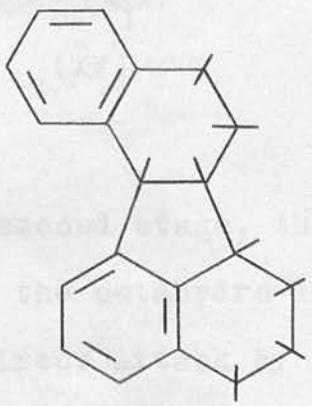


(II)

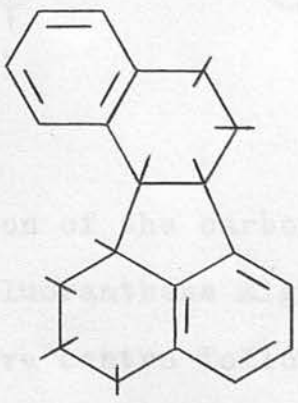
THE ISOMERIC OCTAHYDRO-10,11-BENZFLUORANTHENES.

Structural and Mechanistic Considerations:

There are two schools of thought concerning the structure and mechanism of formation of the octahydro-10,11-benzfluoranthenes. Campbell *et al*. suggested that the hydrocarbon isolated by von Braun and Kirschbaum $C_{20}H_{20}$ (m.p. 93°) was probably 1,2,3,4,9,12,13,14-octahydro-10,11-benzfluoranthene i.e., structure A.



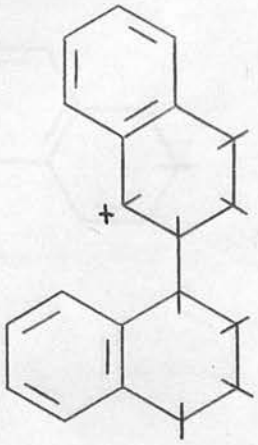
(A)



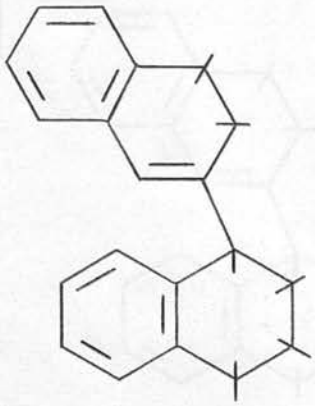
(B)

They visualised the first stage as the polarisation of the ethylenic double bond in the 1,2-dialin thus:-

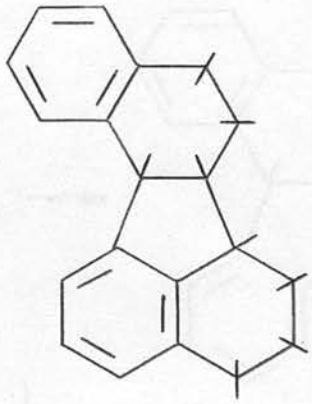
union with a proton would produce the carbonium ion, and interaction of this with the polar compound would give the dimeric carbonium ion (XV).



(XV)



(XVI)



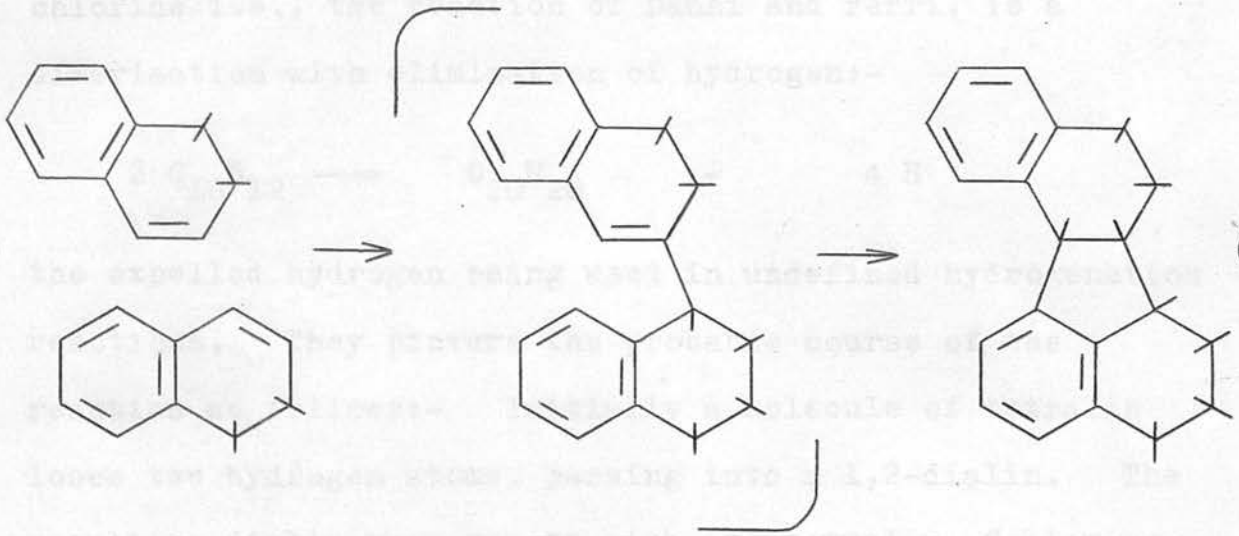
(A)

The second stage, the conversion of the carbonium ion into the octahydro-10,11-benzfluoranthene might be explained by direct attack by the positive centre followed by elimination of a proton, or a proton might first be lost to give the unsaturated hydrocarbon (XVI). Ring-closure would then result from the action of sulphuric acid on the double bond followed by interaction with the other 'half' of the molecule. A similar mechanism has been proposed by Woodward and Eastman (10) to account for a dimerisation in the tetrahydro-naphthalene series.

Nenitzescu and Avram (loc.cit.), suggested that the

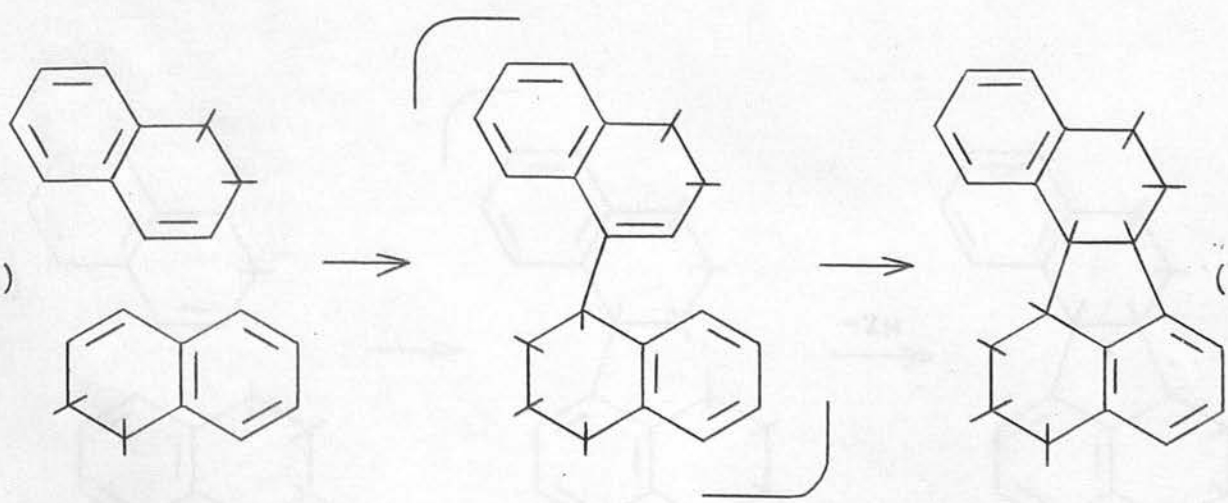
dimerisation of 1,2-dialin under the influence of sulphuric acid (von Braun's reaction), proceeds <u>via</u> one of the following mechanisms (i) and (ii).

(i)



(A)

(ii)



(B)

They prefer scheme (ii), and although they suggest that von Braun's hydrocarbon $C_{20}H_{20}$ (m.p. 93°) will have

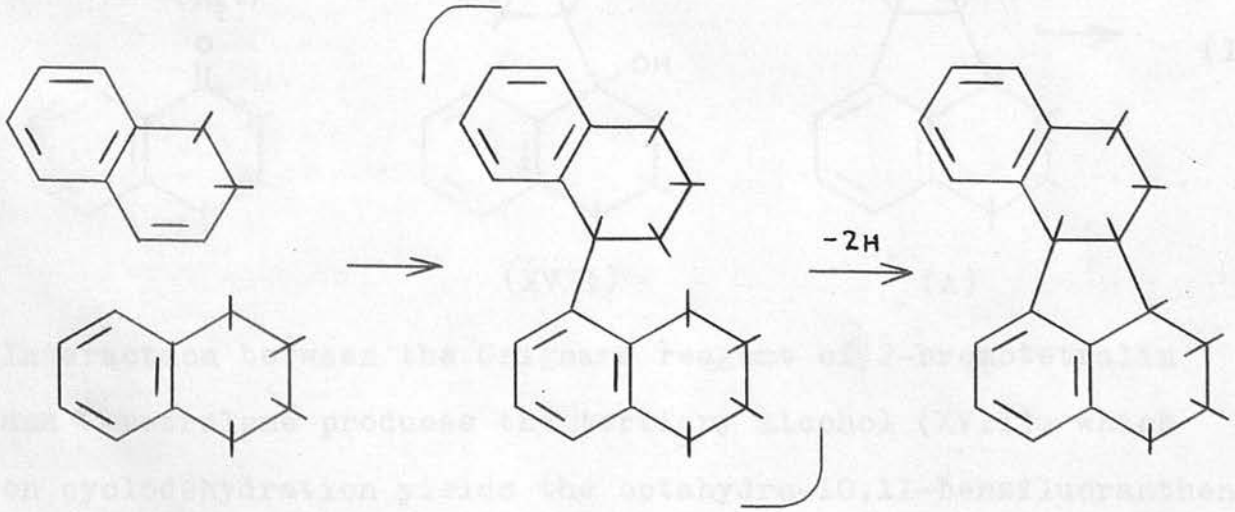
structure B, 5,6,7,8,9,12,13,14-octahydro-10,11-benzfluoranthene, they were unable to prove this by direct synthesis.

They suggest that the transformation which the tetralin molecule undergoes through the influence of aluminium chloride i.e., the reaction of Dansi and Ferri, is a dimerisation with elimination of hydrogen:-

$$2\ C_{10}H_{12} \longrightarrow C_{20}H_{20} + 4\ H$$

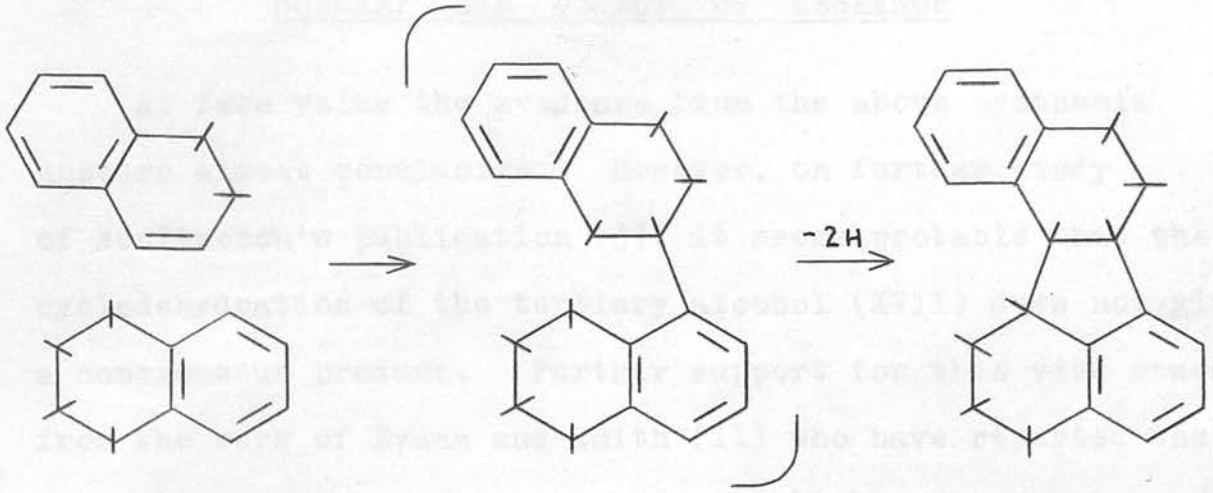
the expelled hydrogen being used in undefined hydrogenation reactions. They picture the probable course of the reaction as follows:- Initially a molecule of tetralin loses two hydrogen atoms, passing into a 1,2-dialin. The resulting dialin then reacts with the tetralin, following one of the mechanisms below.

(iii)



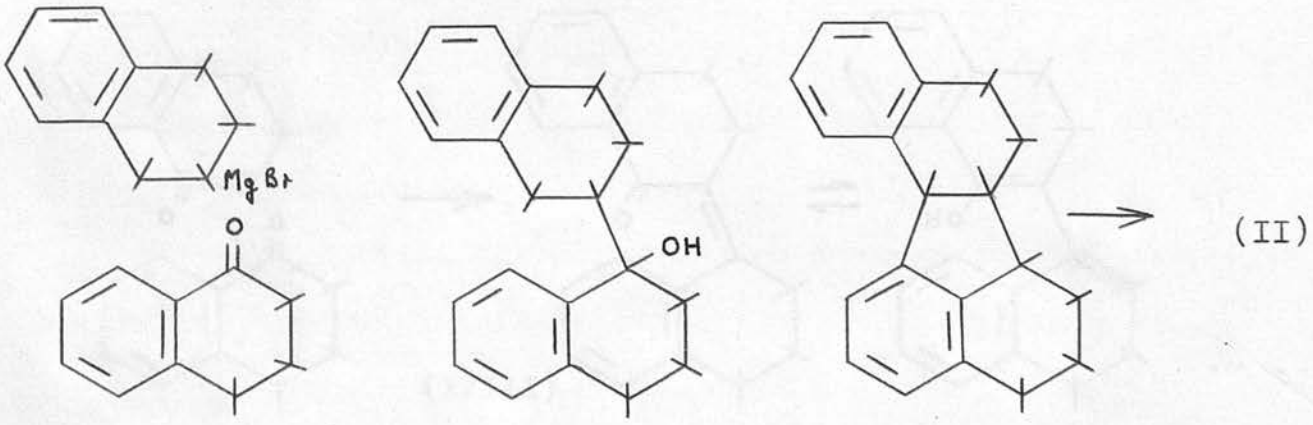
(A)

iv)



(B)

Nenitzescu and Avram propose structure A for Dansi and Ferri's hydrocarbon $C_{20}H_{20}$ (m.p. 150·5°), and support their hypothesis with the following synthesis of A.

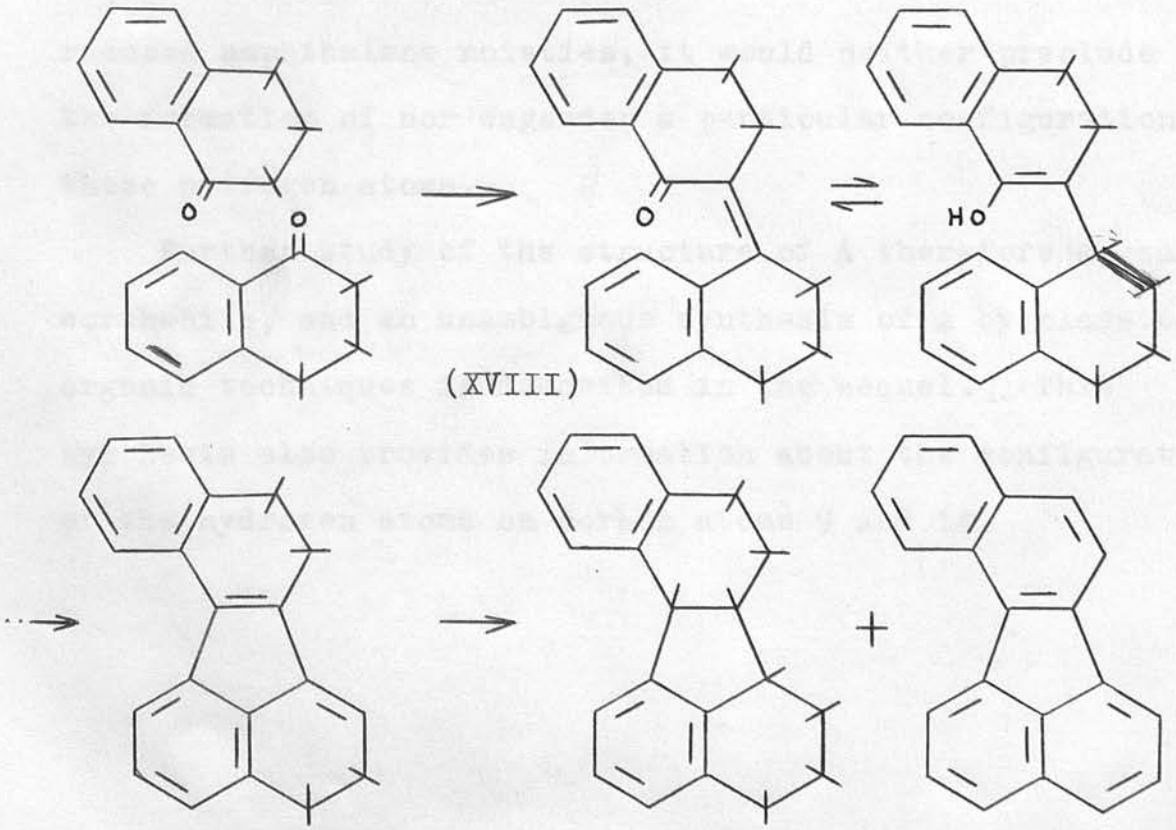


(XVII) (A) (II)

Interaction between the Grignard reagent of 2-bromotetralin and α-tetralone produces the tertiary alcohol (XVII), which on cyclodehydration yields the octahydro-10,11-benzfluoranthene A (m.p. 150·5°). Dehydrogenation of this gave 10,11-benzfluoranthene (II, m.p. 165°, picrate 195°).

SUMMARY AND OBJECT OF RESEARCH

At face value the evidence from the above synthesis appears almost conclusive. However, on further study of Nenitzescu's publication (3), it seems probable that the cyclodehydration of the tertiary alcohol (XVII) does not give a homogeneous product. Further support for this view comes from the work of Evans and Smith (11) who have reported the disproportionation of a tetrahydro-10,11-benzfluoranthene (XIX) in the presence of polyphosphoric acid. They treated α-tetralone at 170° with polyphosphoric acid and isolated 10,11-benzfluoranthene and the hydrocarbon of Dansi and Ferri (A) as products, according to the following scheme:-



(XVIII)

(XIX) (A) (II)

The ketone (XVIII) originally produced reacts in its enol form to give a tetrahydro-10,11-benzfluoranthene (XIX), which then disproportionates into the octahydro-10,11-benzfluoranthene (A), and 10,11-benzfluoranthene (II). From the results of this work, the possibility of disproportionation during Nenitzescu's cyclodehydration reaction cannot be ruled out entirely.

One further factor which Nenitzescu did not consider concerns the stereochemistry of the hydrogen atoms at positions 9 and 14 in the molecule. Each of the substances A and B should be capable of existing in two forms depending on the configuration of these two hydrogen atoms. Since Nenitzescu's synthesis involves the interaction of two reduced naphthalene moieties, it would neither preclude the formation of nor engender a particular configuration of these hydrogen atoms.

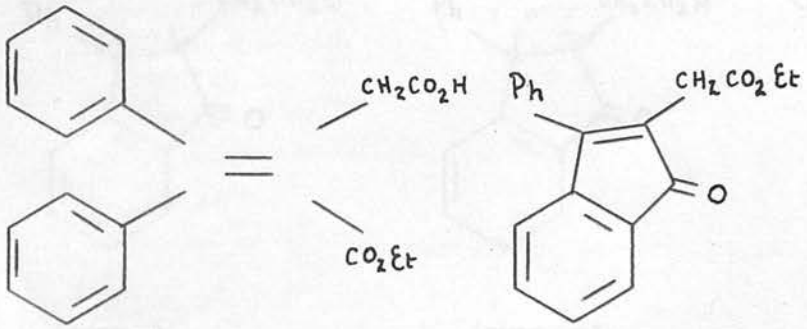
Further study of the structure of A therefore appeared worthwhile, and an unambiguous synthesis of A by classical organic techniques is described in the sequel. This synthesis also provides information about the configuration of the hydrogen atoms om carbon atoms 9 and 14.

PART I

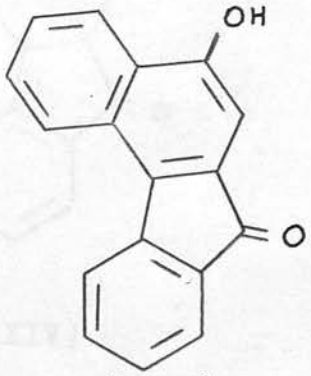
The Unambiguous Synthesis of 1,2,3,4,9,12,13,14-Octahydro-10,11-Benzfluoranthene.

Discussion

The starting point of the synthesis was the readily available ethyl 3-phenylindene-1-one-2-acetate (XXI).



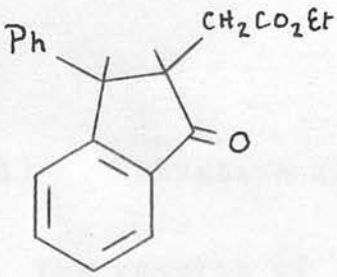
(XX) (XXI)



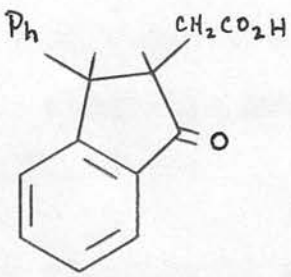
(XXII)

This is prepared via the Stobbé condensation between benzophenone and diethyl succinate, which produces β-carbethoxy-γ,γ-diphenylvinylacetic acid (XX). The half-ester is cyclised by heating in acetic acid containing zinc chloride, and under these conditions we obtain preferential formation of the indenone (XXI), and ethyl 3-phenylindene-1-one-2-acetate is produced in high yield (25), together with a small amount of the corresponding acid, and a trace of the 2-hydroxy-3,4-benzfluorene-9-one (XXII).

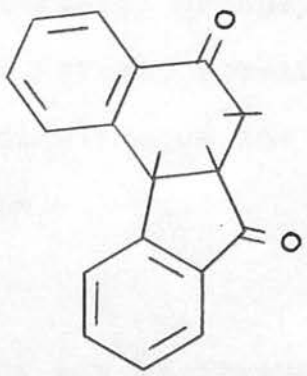
Catalytic hydrogenation of the indenone acetate produced ethyl 3-phenylindan-1-one-2-acetate (XXIa), and this on hydrolysis with 10% aqueous methanolic potassium hydroxide gave the corresponding acid (XXIII).



(XXIa)



(XXIII)



(XXIV)

This acid was cyclised with polyphosphoric acid forming tetrahydro-3,4-benzfluorene-2,9-dione (XXIV) in 30% yield. Koelsch (12) had earlier demonstrated that cyclisation of this acid, prepared by the cyclisation of β-benzoyl-β-benzilidene propionic acid with aluminium chloride, could be performed in concentrated sulphuric acid. This method also gives a yield in the region of 30%, but it gives, however, a cleaner product and has been used during this synthesis.

The next stage in the synthesis was to obtain selective addition to the 5-membered ring ketone. This type of problem is often encountered in Steroid chemistry, and may be overcome in several ways (13). This particular problem was approached with the following experiments in view:-

(i) Reduction: possibility of selective reduction of one of the carbonyl groups.

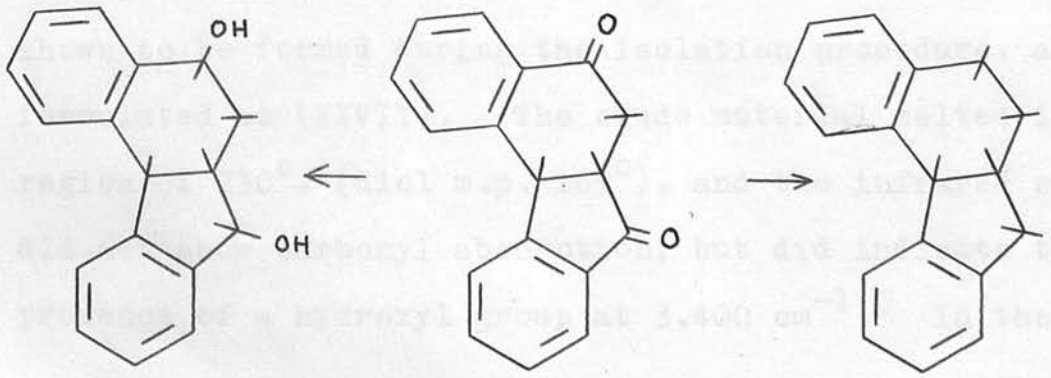
(ii) Oxidation: If the diol was formed, possibility of selective oxidation of one of the alcoholic groups.

(iii) Selective Ketal Formation.

The results of these experiments will now be discussed in detail.

(i) Reduction:

Treatment of the diketone (XXIV) with lithium aluminium hydride in ether, or sodium borohydride in pyridine at room temperature, produced the corresponding diol (XXV). Catalytic reduction with Adams catalyst gave a mixture of the hydrocarbon (XXVI) and a small amount of the diol (XXV).

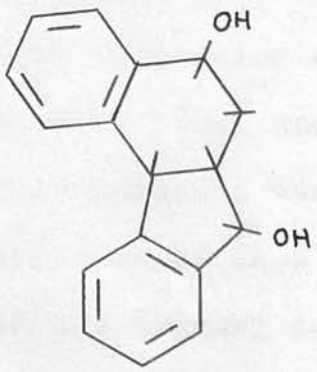


(XXV) (XXIV) (XXVI)

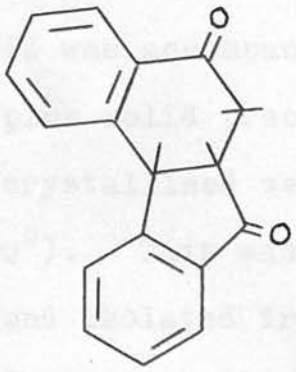
These results indicated that differentiation between the two carbonyl groups by reductive procedures, is not readily achieved.

(ii) Oxidation:

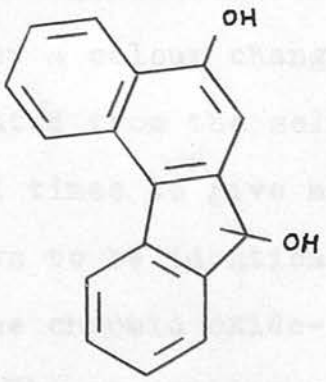
The possibility of selective oxidation of one of the alcoholic groups in the diol (XXV) was investigated. Room temperature oxidation with the chromic oxide-pyridine reagent (14) yielded two products. The major product was the diketone (XXIV).



(XXV)



(XXIV)

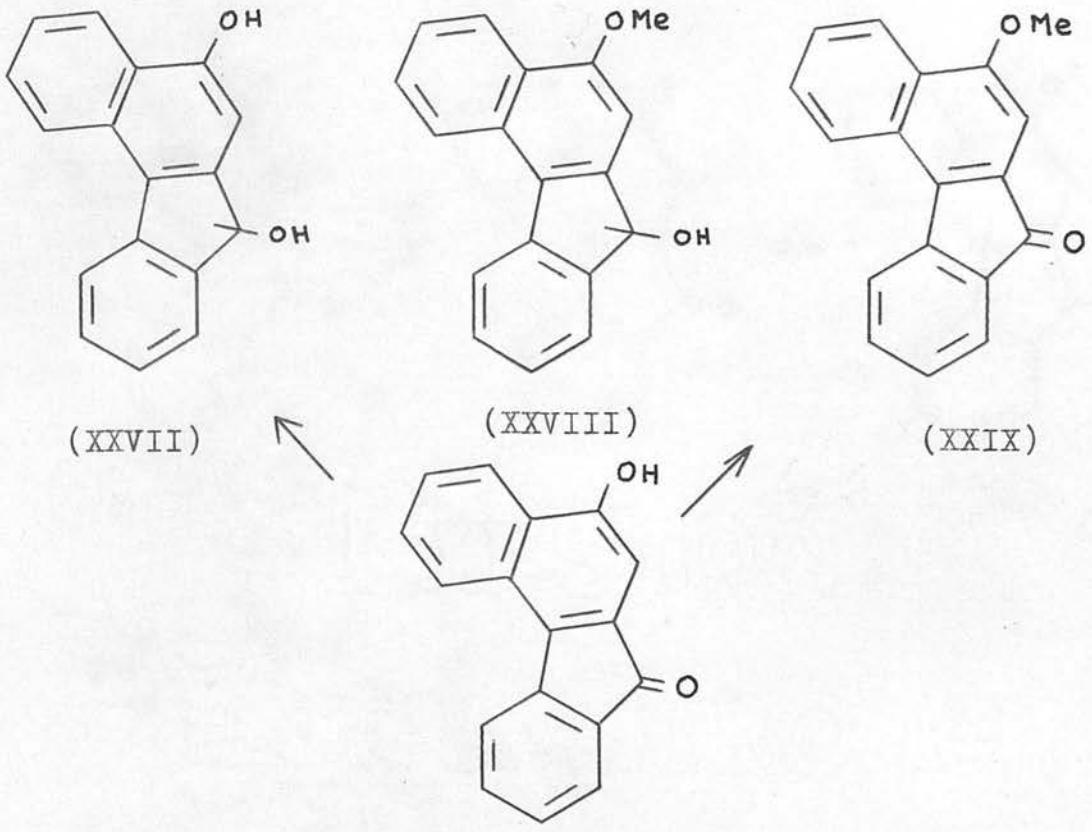


(XXVII)

The other product, isolated in small yield, was subsequently shown to be formed during the isolation procedure, and is formulated as (XXVII). The crude material melted in the region of 230°, (diol m.p. 169°), and the infrared spectrum did not show carbonyl absorption, but did indicate the presence of a hydroxyl group at 3,400 cm^{-1}. In the work-up

of this reaction, the chromic-pyridine complex was destroyed by addition of excess dilute sodium hydroxide. This developed a deep-blue colouration, and the hydroxy compound was ultimately isolated from the aqueous alkaline fraction. From the results of this work hopes of gaining a differentiation between the two carbonyl or the two alcoholic groups had to be abandoned. The formation and structure of the unexpected hydroxy compound had still to be explained.

Treatment of the diketone with 2N methanolic sodium hydroxide produced a deep-blue solution. Acidification with hydrochloric acid was accompanied by a colour change blue to pink, and a pink solid precipitated from the solution. This material was recrystallised several times to give a white solid (m.p. 250°). This was shown to be identical to the hydroxy compound isolated from the chromic oxide-pyridine oxidation of the diol (XXV). The properties of this substance indicated the presence of a phenolic hydroxyl group. The high melting point, coupled with the fact that the ultra-violet spectrum resembled that of a benzfluorene, suggested that both carbonyl groups had enolised to form 2,9-dihydroxy-3,4-benzfluorene (XXVII). The analysis was in accord with this structure, which was confirmed as follows:-



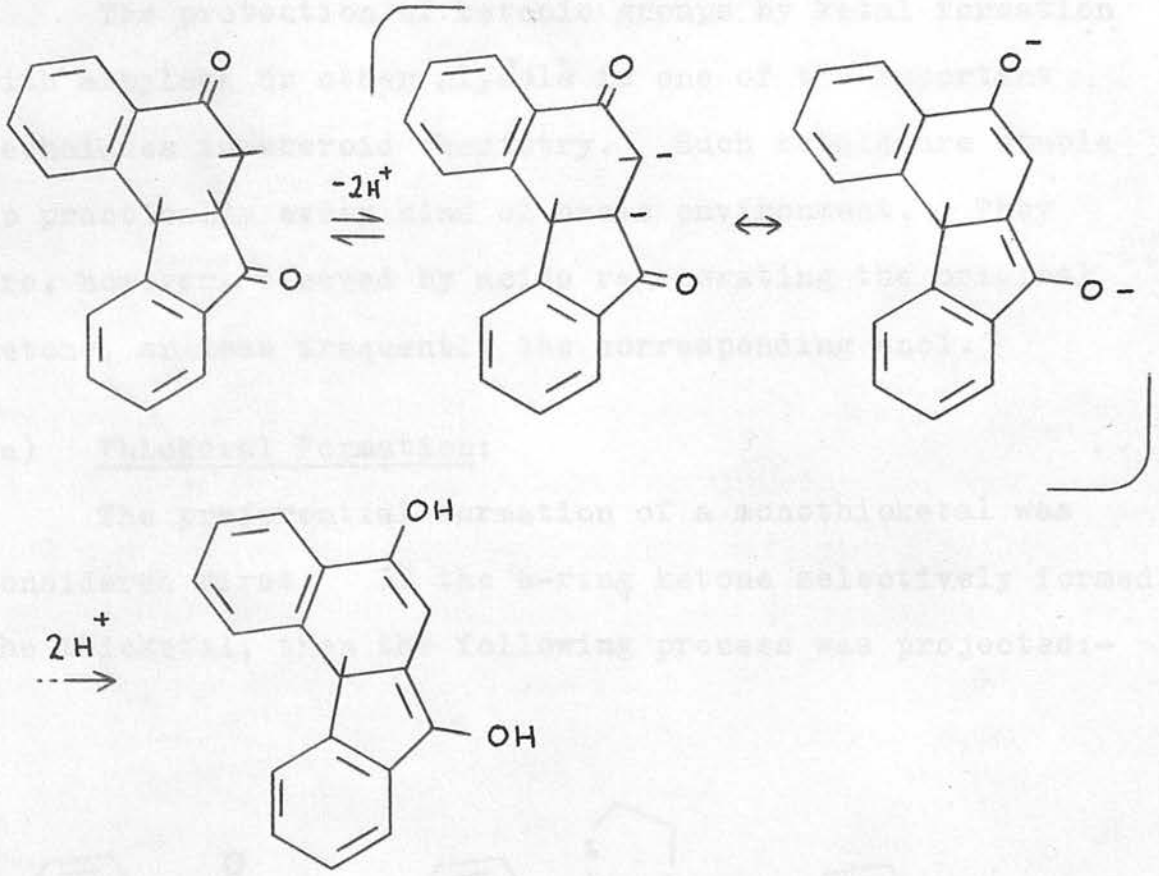
(XXVII) (XXVIII) (XXIX)

(XXII)

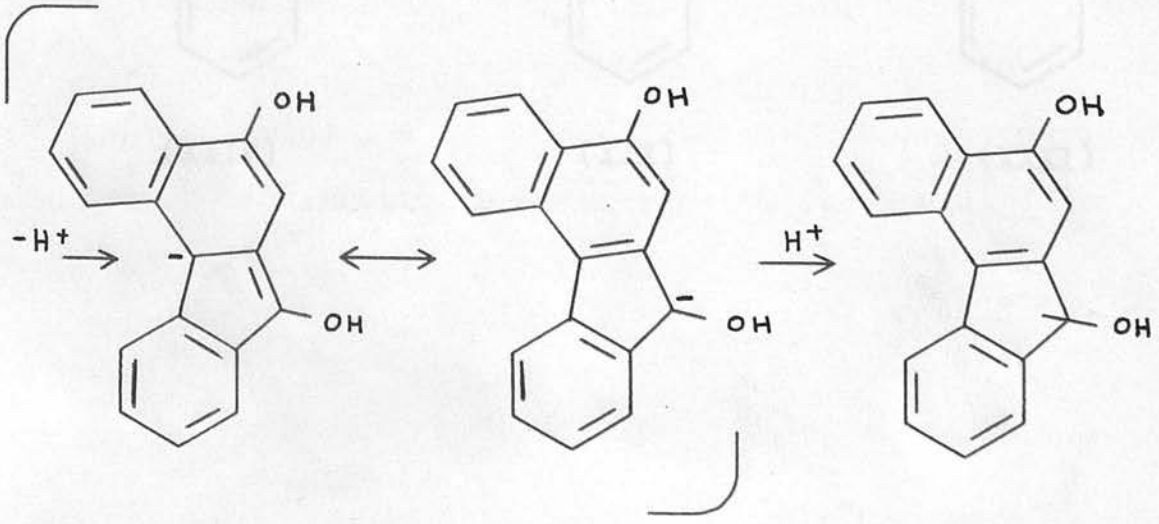
Treatment of the dihydroxy-3,4-benzfluorene (XXVII) with dimethyl sulphate in sodium hydroxide solution produced the methyl ether (XXVIII), which on oxidation with chromic oxide-pyridine reagent produced 2-methoxy-3,4-benzfluorene-9-one (XXIX). The compounds (XXVII) and (XXIX) were shown to be identical to the products obtained from 2-hydroxy-3, 4-benzfluorene-9-one by reduction with lithium aluminium hydride and methylation with dimethyl sulphate respectively.

This rearrangement is most easily visualised as taking place in two stages:-

(a) Formation of the corresponding di-enol.



(b) Removal of a proton from the di-enol, rearrangement of the carbanion to a more thermodynamically stable structure, and finally addition of a proton to give the product.

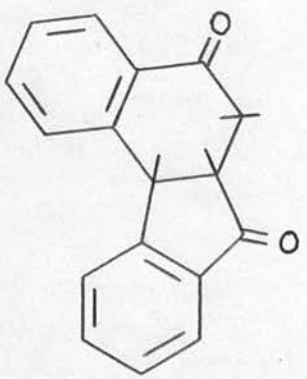


(iii) Selective Ketal Formation:

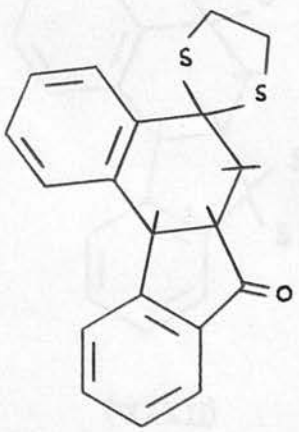
The protection of ketonic groups by ketal formation with ethylene or other glycols is one of the important techniques in steroid chemistry. Such ketals are stable to practically every kind of basic environment. They are, however, cleaved by acids regenerating the original ketone, or less frequently the corresponding enol.

(a) Thioketal Formation:

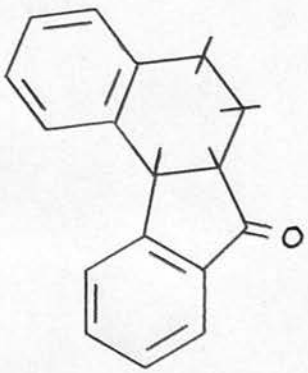
The preferential formation of a monothioketal was considered first. If the 6-ring ketone selectively formed the thioketal, then the following process was projected:-



(XXIV)



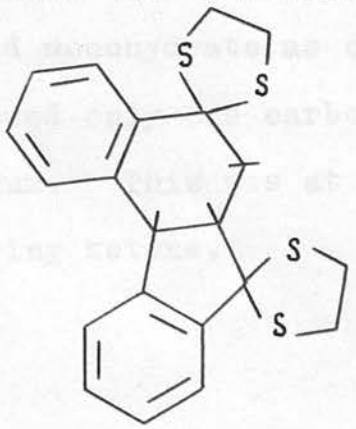
(XXX)



(XXXI)

Sulphur extrusion of the monothioketal (XXX) would give the monoketone (XXXI). This would then allow uncomplicated introduction of a side-chain to the carbonyl group at the 9-position. Since the infrared spectrum of the diketone (XXIV) shows two carbonyl absorption peaks at 1715 cm^{-1}. (5-ring ketone) and 1685 cm^{-1}. (6-ring ketone), examination of the spectrum of the product would indicate which carbonyl group had ketalised.

When an ethereal suspension of the diketone was treated with one molecule of ethane dithiol, with boron trifluoride etherate as catalyst, a mixture of the dithioketal (XXXII) and the unchanged diketone was isolated.



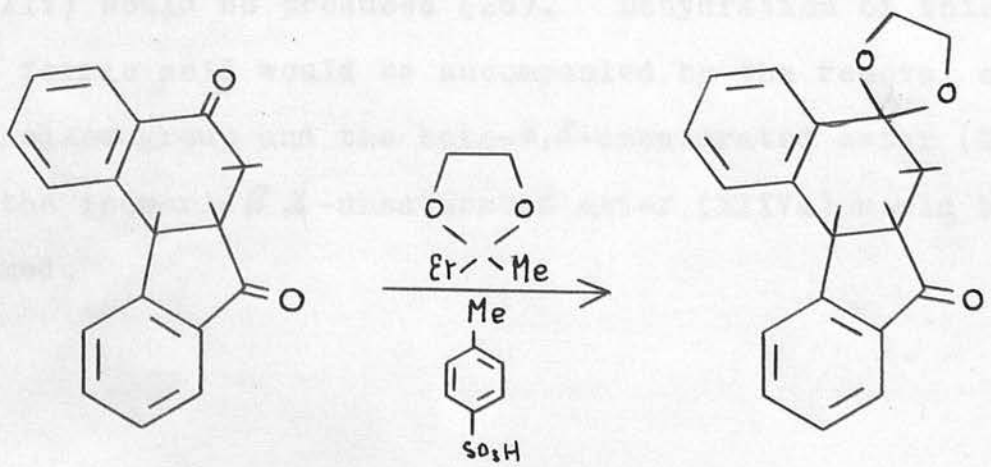
(XXXII)

When two molecules of ethane dithiol were introduced, the dithioketal was produced in quantitative yield. This route was therefore abandoned.

(b) Glycol Ketal Formation:

Most procedures for ketalisation with ethylene glycol follow the original method of Salmi (15). This involves refluxing the ketone in benzene or toluene with excess glycol in presence of an acid catalyst, with azeotropic removal of the water formed. However, increased selectivity of ketalisation is possible by using the method of exchange ketalisation (16) between a ketone and the ketals of 2-butanone, in the presence of acid catalysts. This was the method used in this work.

When the diketone was refluxed for several hours with excess 2-butanone ethylene ketal, containing a trace of p-toluenesulphonic acid monohydrate as catalyst, a substance was isolated which showed only one carbonyl absorption peak in the infrared spectrum. This was at 1715 cm^{-1}. and corresponds to the 5-ring ketone.



(XXIV) (XXXIII)

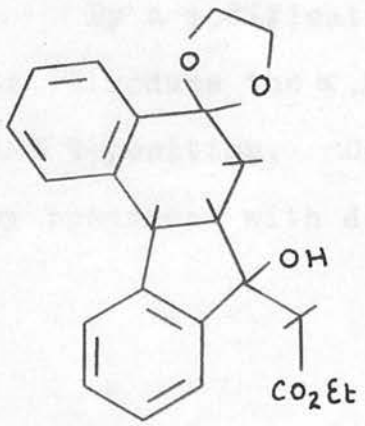
It thus appeared that the 6-ring ketone had selectively undergone the exchange reaction to give the dioxolane-ketone (XXXIII). Exchange dioxolanation appears to be more subject to steric and electronic effects than direct dioxolanation, and this may explain why the 6-membered ring ketone selectively undergoes exchange.

In view of the alkali induced enolisation and subsequent aromatisation of the diketone (XXIV) previously discussed, the presence of the alkali stable dioxolane group in the 2-position appeared most suitable, as it would render further rearrangement of this type unlikely.

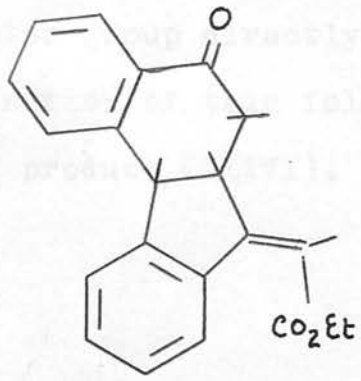
The next step to be considered in the development of the synthesis was the introduction of a suitable side-chain at the 9-position. This was approached with the following experimental techniques in mind.

1. Reformatsky Reaction:

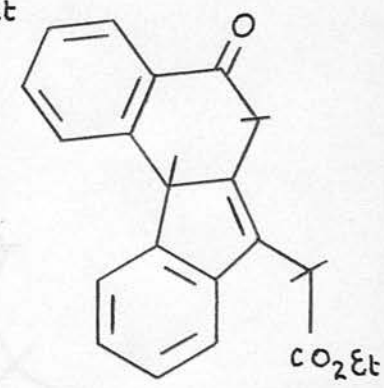
With zinc and ethyl bromoacetate the hydroxy-ester (XXXIV) would be produced (26). Dehydration of this with 90% formic acid would be accompanied by the removal of the dioxolane group and the keto-α,β-unsaturated ester (XXXV) or the isomeric β,γ-unsaturated ester (XXXVa) would be formed.



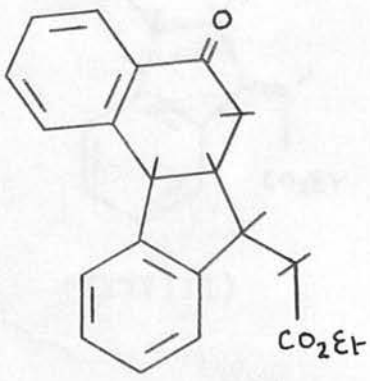
(XXXIV)



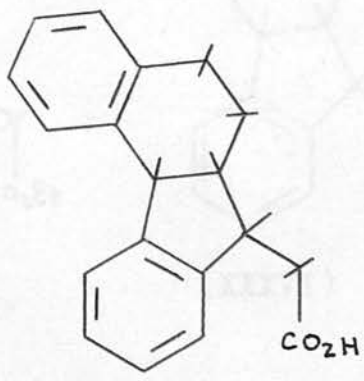
(XXXV)



(XXXVa)



(XXXVI)

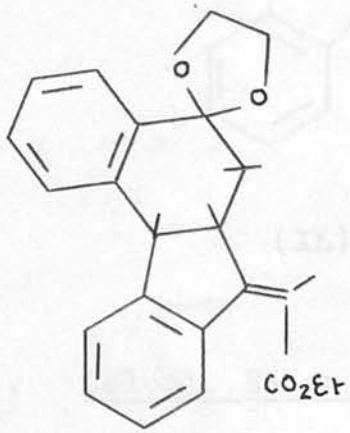


(XXXVII)

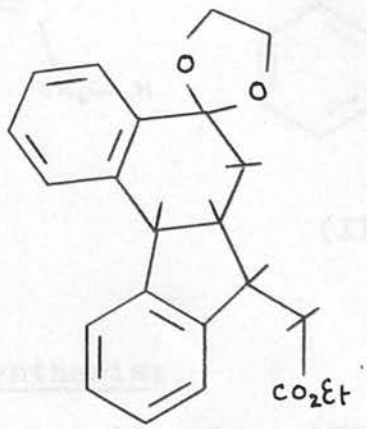
Catalytic hydrogenation to give (XXXVI), followed by Wolff-Kishner reduction would produce the saturated acid (XXXVII). The synthesis could then be completed by Arndt-Eistert chain extension, cyclisation to the cyclic ketone, then reduction to give the octahydro compound.

2. Wittig Synthesis:

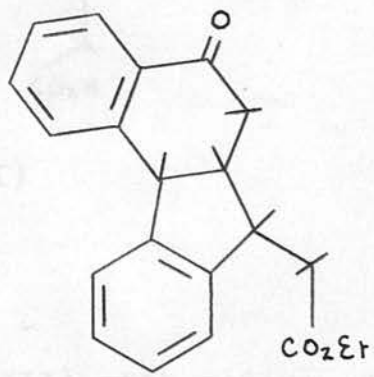
By a modification of this reaction it would be possible to introduce the α,β-unsaturated ester group directly into the 9-position. Catalytic hydrogenation of this followed by treatment with dilute acid would produce (XXXVI).



(XXXVIII)



(XXXIX)



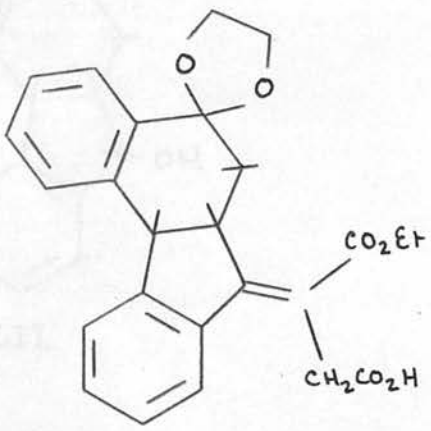
(XXXVI)

The synthesis could then be continued as in one above.

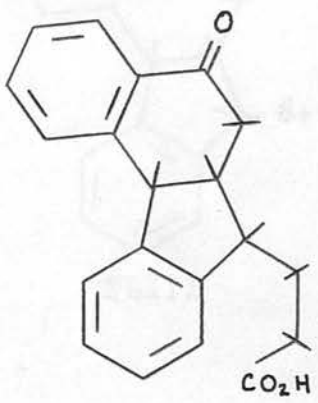
3. Stobbé Reaction:

Condensation of the ketodioxolane (XXXIII) with diethyl succinate in potassium-tert-butoxide would produce the half-ester or isomeric half-ester (XL). This could

be converted into the keto-acid (XLI), and the synthesis completed as in one above.



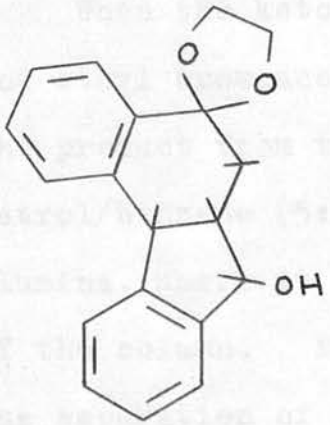
(XL)



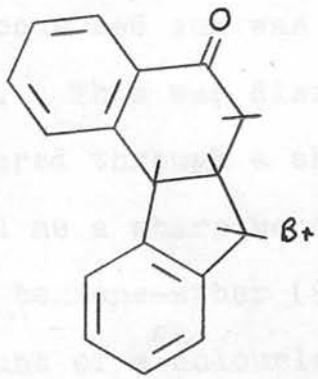
(XLI)

4. Malonic Ester Synthesis:

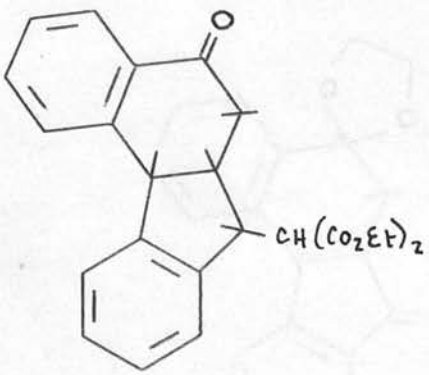
Reduction of the ketodioxolane (XXXIII) with sodium borohydride would give the dioxolane alcohol (XLII), and this with phosphorus tribromide in ether would produce the corresponding bromide (XLIII). Treatment of the bromide with sodiomalonic ester would yield (XLIV). Hydrolysis and decarboxylation would give the keto-acid (XLV) which could be developed as in one above.



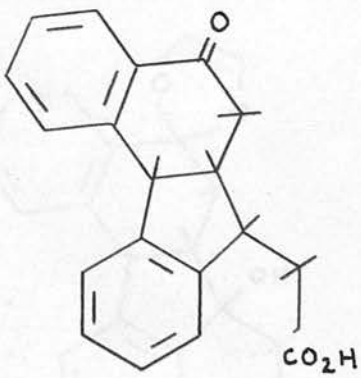
XLII



XLIII



XLIV

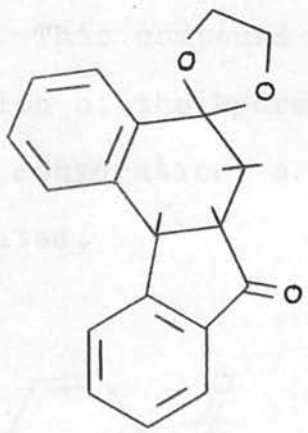


XLV

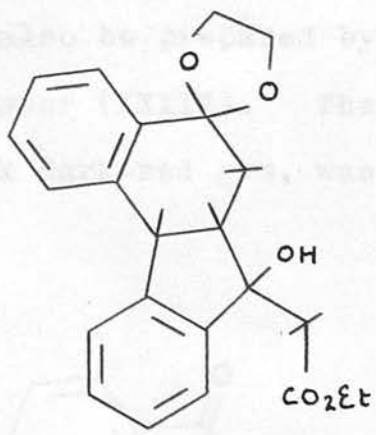
With the exception of this last route, these syntheses could be carried out in neutral or basic media. The experimental results will now be discussed in detail.

The Reformatsky Reaction.

When the ketodioxolane (XXXIII) was treated with zinc and ethyl bromoacetate, a viscous red gum was isolated as the product from the reaction. This was dissolved in petrol/benzene (5:1) and filtered through a short column of alumina, where it was adsorbed as a sharp band at the top of the column. Elution with benzene-ether (9:1) caused the separation of a small amount of a colourless oil. This crystallised from petrol(60/80°) as colourless needles (m.p. 161-3°). The infrared spectrum of this compound



(XXXIII)

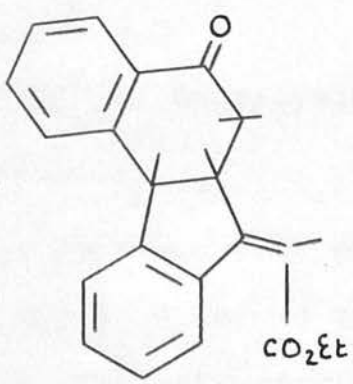


(XXXIV)

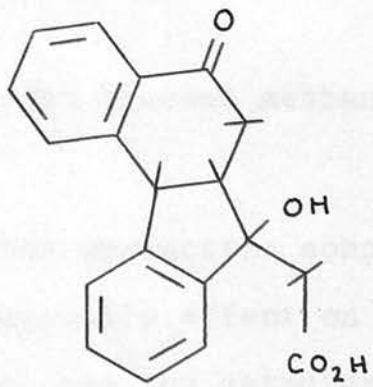
showed peaks at 3550 cm^{-1}. (-OH) and 1735 cm^{-1}. (C=O of saturated ester). It is formulated as (XXXIV) and the analysis supports this structure. The major portion of

the product, a red gum, was obtained by 'stripping' the column with ether-methanol (5%). This material did not crystallise from the usual range of solvents. Portions of this gum were subjected to acid dehydration and alkaline hydrolysis.

A portion of the above gum was heated with 90% formic acid, and a small amount of a colourless solid (plates m.p. 146-8°) was isolated from the reaction products. The infrared spectrum of this material showed no hydroxyl absorption, but did show absorption peaks at 1710 cm^{-1}. (α,β-unsaturated ester); 1685 cm^{-1}. (6-ring ketone) and 1655 cm^{-1}. (C=C). The analysis agrees with the structure (XXXV). This compound may also be prepared by formic acid dehydration of the hydroxy ester (XXXIV). The major product from the dehydration, a thick dark-red gum, was not further investigated.



(XXXV)



(XLVI)

Alkaline hydrolysis of the remaining portion of the Reformatsky gum produced a mixture of acids. This was separated by fractional crystallisation into two components:-

(i) A small amount of colourless silky needles (m.p. 214° decomp.). The analysis and infrared spectrum of this material, 3450 cm^{-1}. (OH), 1700 cm^{-1}. (CO_2H), 1670 cm^{-1}. (C=O), corresponds to the structure (XLVI).

(ii) The second and major component of the mixture is also a colourless solid (plates m.p. 206° decomp.). The infrared spectrum of this material shows three absorption peaks in the carbonyl region. It is probably still impure, and its constitution has not been established.

From the results of the above experiments it was evident that the dioxolane group was being removed from the 2-position. This could have taken place:

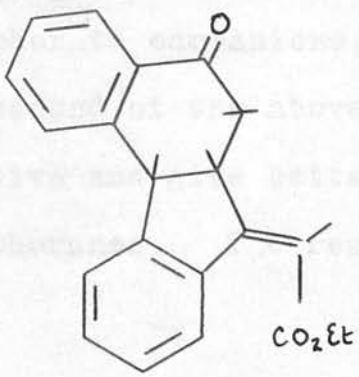
(i) During the course of the Reformatsky reaction.

(ii) During the acid decomposition of the organozinc complex.

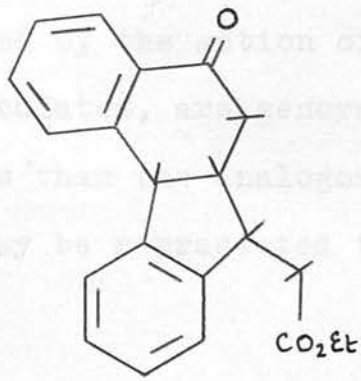
(iii) During the hydrolysis with aqueous methanolic hydroxide.

Since decomposition of the organozinc complex with ammonium chloride had no discernable effect on the products from the Reformatsky reaction, and the ketodioxolane (XXXIII) was recovered unchanged after two hours reflux with aqueous

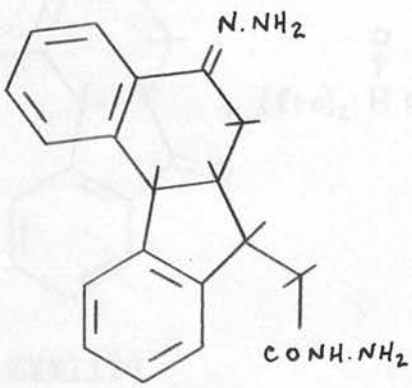
methanolic hydroxide, it was concluded that the dioxolane group was being expelled during the course of the Reformatsky reaction. Owing to this complication, this synthetic route had to be discarded. From the above experiments, however, a small amount of the keto-unsaturated ester (XXXV) was obtained. This on catalytic hydrogenation gave the saturated keto-ester (XXXVI).



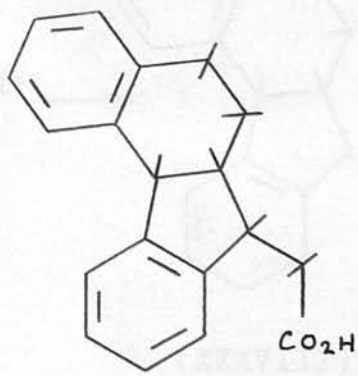
(XXXV)



(XXXVI)



(XLVII)

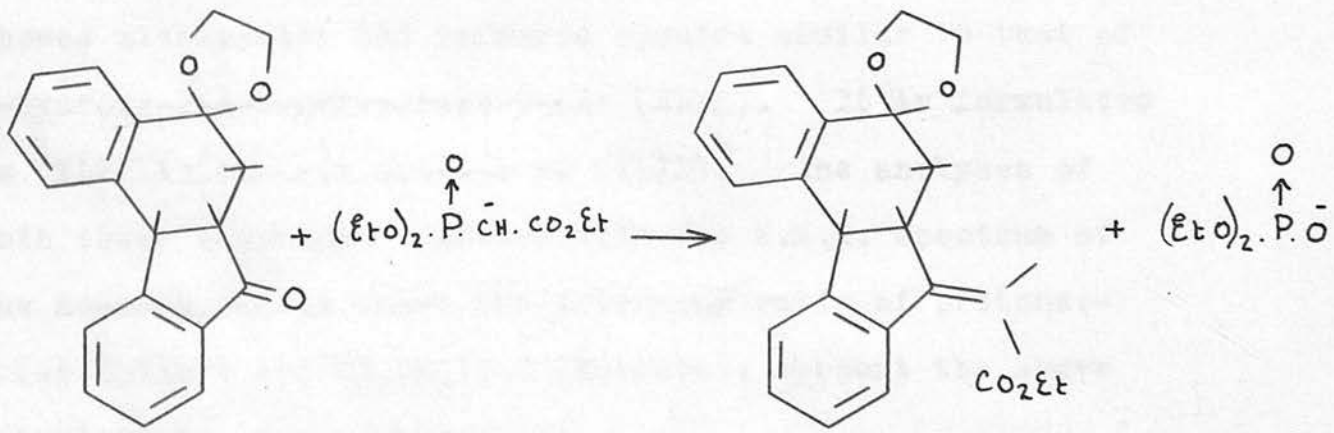


(XXXVII)

Wolff-Kishner reduction of the corresponding hydrazone-hydrazide produced a few crystals of a saturated acid (m.p. 216-8° decomp.). This was shown to be identical to (XXXVII) prepared in a later part of this work.

The Wittig Reaction.

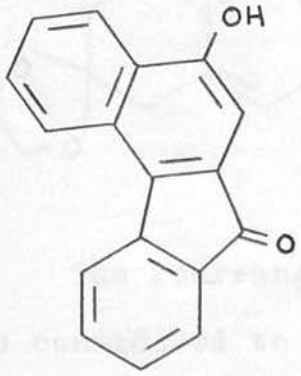
By means of a modification of this reaction, it is possible to replace carbonyl by the α,β-unsaturated ester group. This may be carried out by using intermediates such as carboethoxymethyltriphenylphosphonium bromide, $Ph_3.P.CH_2CO_2EtBr$ (27) or triethylphosphonoacetate, $(EtO)_2P.CH_2CO_2Et$. Wadsworth and Emmons (17) have shown that the phosphonate carbanions, prepared by the action of base on the second of the above intermediates, are generally more reactive and give better yields than the analogous triarylphosphoranes. The reaction may be represented thus:-



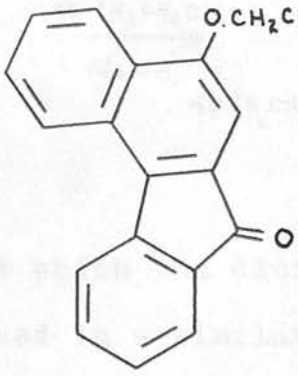
(XXXIII) (XXXVIII)

The phosphonate carbanion may be conveniently prepared by treating a solution of triethylphosphonoacetate in

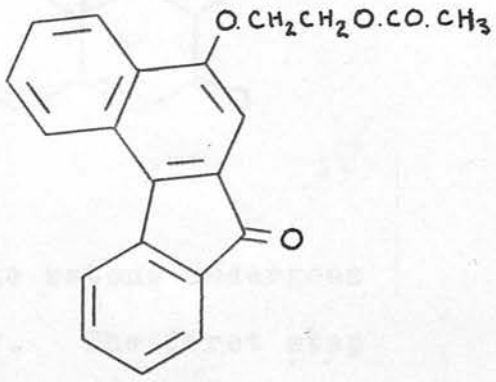
anhydrous ethylene glycol dimethyl ether with sodium hydride.



(XXII)



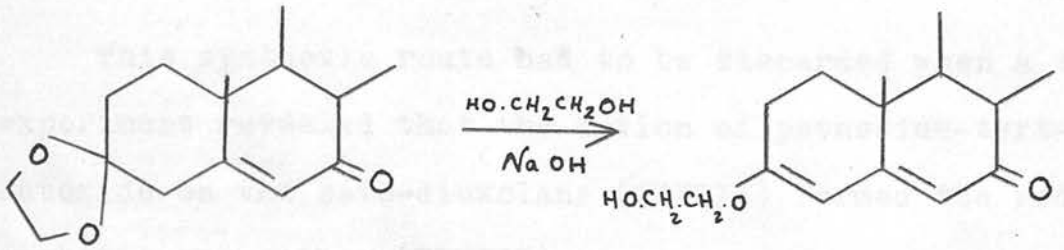
(XLVIII)



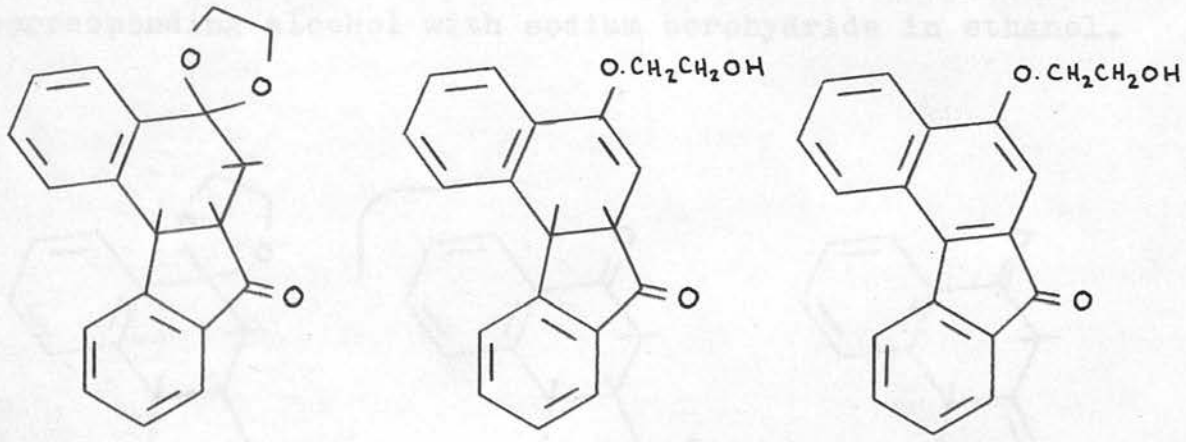
(XLIX)

A soon as the carbonyl compound was introduced into the reaction, the mixture became dark red, and a dark-red solid was ultimately isolated as the product. This material showed ultraviolet and infrared spectra similar to that of 2-hydroxy-3,4-benzfluorene-9-one (XXII). It is formulated as (XLVIII) and its acetate as (XLIX). The analyses of both these compounds together with the N.M.R. spectrum of the acetate, which shows the following ratio of protons:- 9 (aromatic): 4($O \cdot CH_2CH_2$): 3 (acetate), support the above formulations (XLVIII and XLIX).

Lenhard and Bernstein (18) and Rao and Kurath (19) have observed that ethylene ketals undergo ring fission in non-aqueous alkaline media yielding ethylene glycol enol ethers, in cases where they become part of a vinylogous β -diketone system.



The rearrangement which the dioxolane ketone undergoes is considered to proceed in a similar way. The first step



(XXXIII) (L) (XLVIII)

is visualised as ring fission of the dioxolane ring with the formation of the enol ether (L).

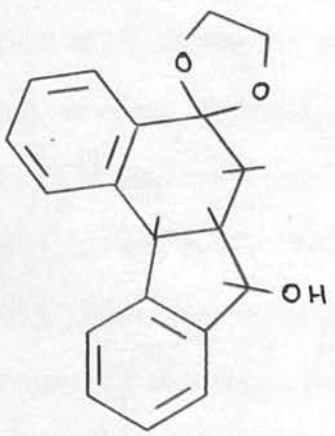
The driving force for the molecule to become fully aromatic and hence more stable, will promote the elimination of two protons, which yields the product (XLVIII).

The Stobbé Condensation.

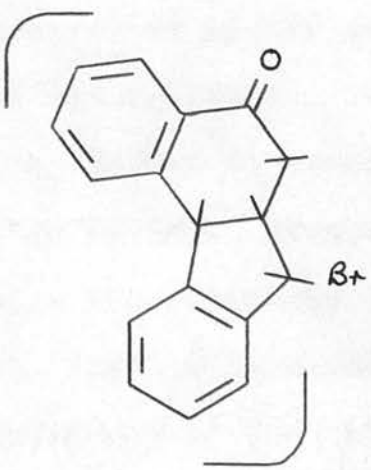
This synthetic route had to be discarded when a test experiment revealed that the action of potassium-tert-butoxide on the keto-dioxolane (XXXIII) formed the red aromatic keto-ether (XLVIII).

Malonic Ester Synthesis.

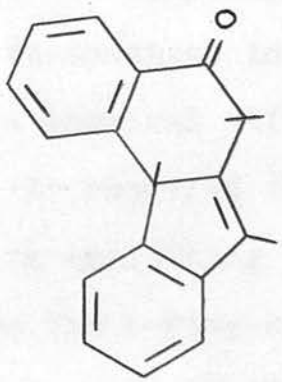
The keto-dioxolane (XXXIII) was reduced to the corresponding alcohol with sodium borohydride in ethanol.



(XLII)



(XLIII)

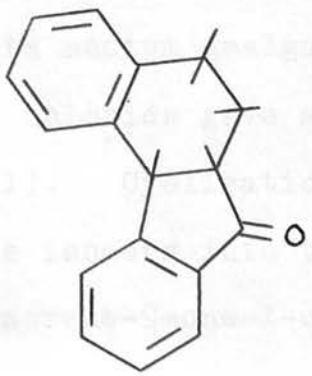


(LI)

The alcohol was treated with phosphorus tribromide in dry ether at 0^{o}, and the reaction appeared to proceed smoothly. However, on working up dehydrobromination occurred. The infrared spectrum and the analysis of the

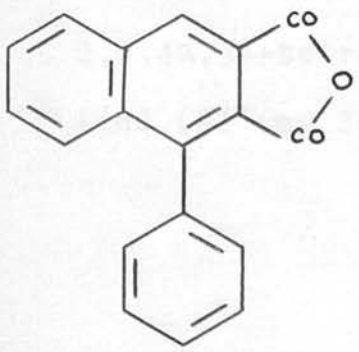
product was in accord with the structure (LI). The instability of the bromide necessitated the rejection of this synthetic approach.

From the experience gained in the above reactions, it appeared that direct addition to the carbonyl group in the keto-dioxolane introduced complications which rendered untenable this synthetic approach. That the 6-ring ketone should be regenerated, and consequently compete with the 5-ring ketone during the Reformatsky reaction was unexpected. Even more surprising was the facile ring opening of the dioxolane group, under non-aqueous alkaline conditions. This was further complicated by the subsequent dehydrogenation and aromatisation of the molecule. The fundamental importance of the keto-dioxolane is that it permits a chemical differentiation between the two carbonyl groups. It appeared that the only hope of extending the synthesis lay in exploiting this property to the full, that is to eliminate the 6-ring ketone and undertake the synthesis of the tetrahydro-3,4-benzfluorene-9-one (XXXI).

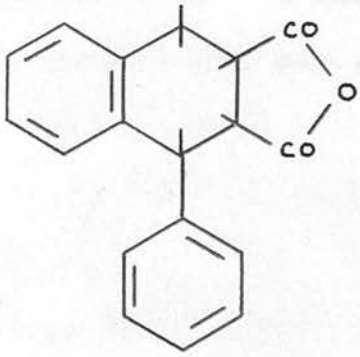


(XXXI)

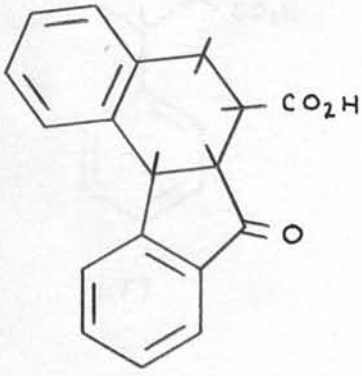
Haworth and Woodcock (20) claimed to have prepared two isomeric forms of 1,2,4^{a},9^{a}-tetrahydro-3,4-benzfluorene-9-one.



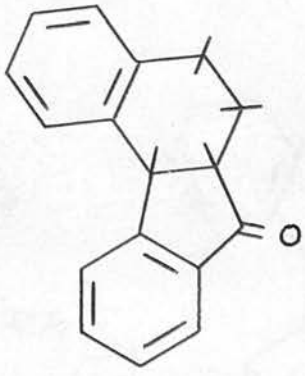
(LII)



(LIII)



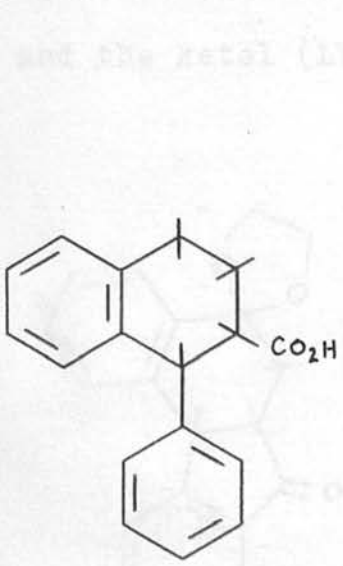
(LIV)



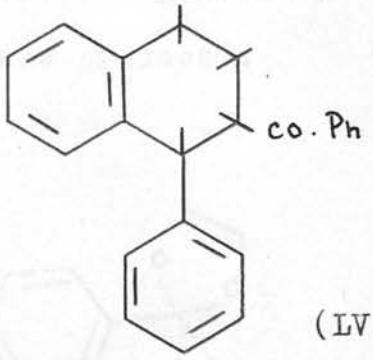
(XXXI)

Reduction of (LII) with sodium amalgam followed by anhydride formation with acetyl chloride gave a mixture of four stereoisomers of (LIII). Cyclisation with aluminium chloride converted the isomers into the corresponding tetrahydro-3,4-benzfluorene-9-one-1-carboxylic acid (LIV).

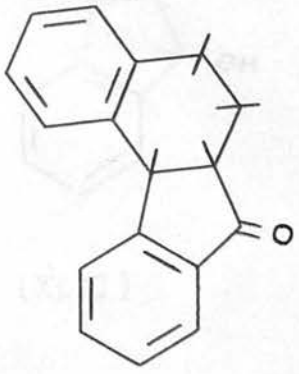
Decarboxylation then gave two tetrahydro-3,4-benzfluorene-9-one isomers (XXXI). They reported that this decarboxylation required further investigation, and when they repeated this experiment, no decarboxylation could be effected. Hence little value can be placed on these results. A small amount of 1,2,4a,9a-tetrahydro-3,4-benzfluorene-9-one was prepared by Kidd (21) as follows.



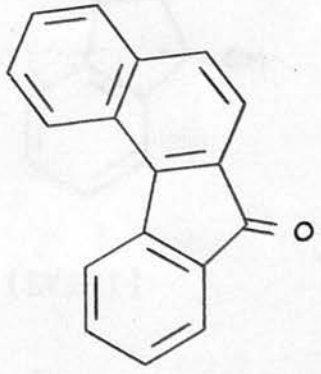
(LV)



(LVI)



(XXXI)

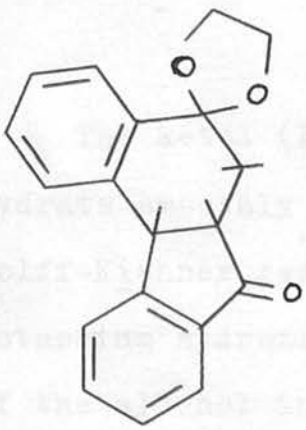


(LVII)

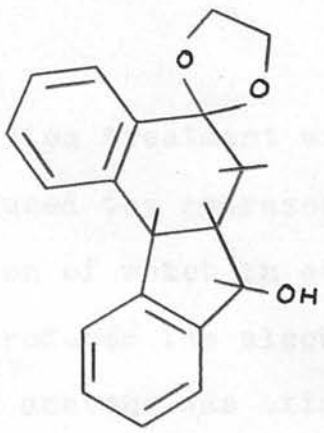
Ring closure of the 1-phenyl-1,2,3,4-tetrahydro-1-naphthoic acid (LV) to give the required ketone (XXXI) proved difficult. With aluminium chloride in benzene, linkage with the solvent occurred (LVI) being formed. With sym-tetrachloroethane a

small amount of the tetrahydro-ketone (XXXI) was isolated, the melting-point of which, (105-6°), is 12° lower than that isolated during the course of this work. This may be due to the presence of 3,4-benzfluorene-9-one, (LVII).

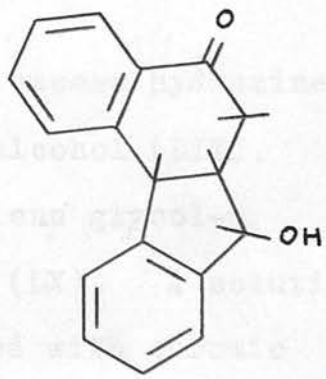
The dioxolane ketone (XXXIII) on reduction with sodium borohydride in absolute ethanol gave the corresponding alcohol (XLII), which on heating with a mixture of acetic acid:methanol:water (1:1:1) regenerated the 6-ring ketone, and the ketol (LVIII) was produced.



(XXXIII)



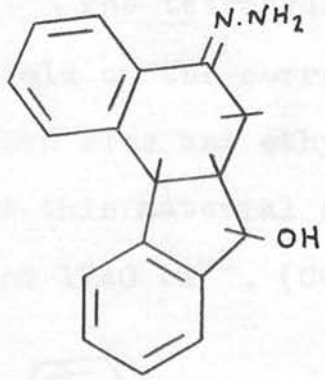
(XLII)



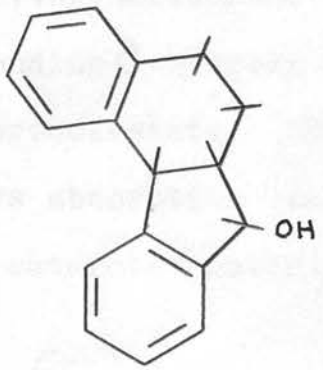
(LVIII)

With the isolation of the ketol, it was now possible to consider reduction of the carbonyl group without affecting the alcohol at position 9. Oxidation of the alcohol would then give the tetrahydro-3,4-benzfluorene-

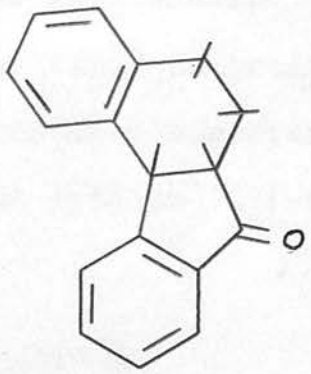
9-one (XXXI). This was carried out as follows:-



(LIX)



(LX)



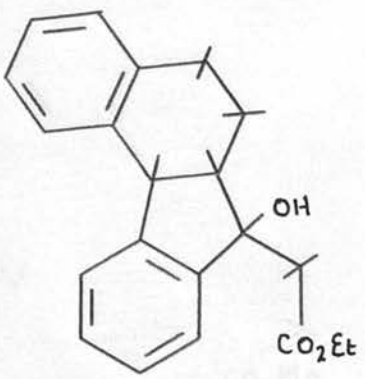
(XXXI)

The ketol (LVIII) on treatment with excess hydrazine hydrate smoothly produced the hydrazone alcohol (LIX), Wolff-Kishner reduction of which in ethylene glycol-potassium hydroxide produced the alcohol (LX). A solution of the alcohol in dry acetone was oxidised with chromic oxide-8N sulphuric acid (22) at 0^{o}. This gave 1,2,4a,9a-tetrahydro-3,4-benzfluorene-9-one (XXXI) in 30% overall yield from the dioxolane ketone (XXXIII). The infrared spectrum of this material showed absorption in the carbonyl region at 1715 cm^{-1}. (5-ring ketone conjugated with an aromatic ring).

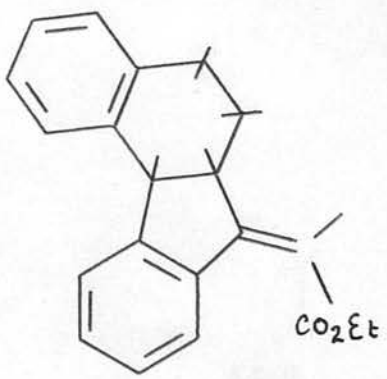
The way now lay open for the straightforward introduction of a side chain at the 9-position. The Reformatsky

reaction was again chosen for this procedure, and it was visualised that the synthesis might be developed as discussed on page 27.

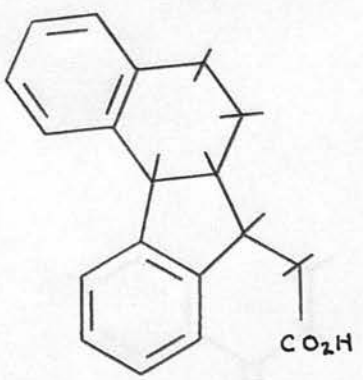
The tetrahydro-3,4-benzfluorene-9-one gave a high yield of the corresponding β-hydroxy ester (LXI) on treatment with zinc and ethyl bromoacetate. The infrared spectrum of this material shows absorption peaks at 3550 cm^{-1}. (-OH) and 1740 cm^{-1}. (C=O, saturated ester).



(LXI)



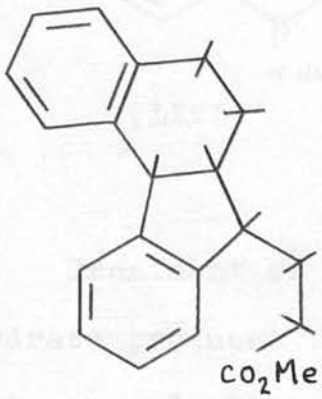
(LXII)



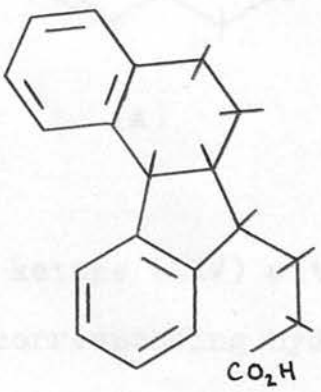
(XXXVII)

Dehydration with 90% formic or acetic acid containing a trace of concentrated hydrochloric acid gave the unsaturated ester (LXII). Reduction with an Adams catalyst gave the saturated ester and this on hydrolysis with methanolic potassium hydroxide produced the corresponding acid (XXXVII). This material was shown to be identical to that isolated during an earlier part of this work (page 34). The Arndt-Eistert reaction was carried out employing the conditions of Bachmann and Sheehan (23). The acid chloride of (XXXVII)

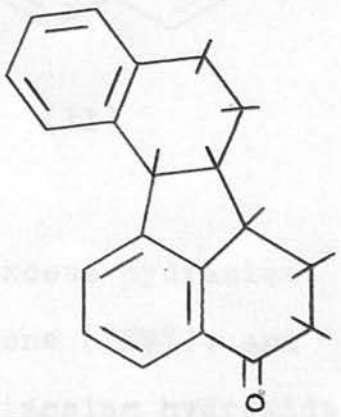
was suspended in ether and treated with excess diazomethane, in the same solvent. The diazo-ketone so obtained was suspended in absolute methanol and decomposed with silver oxide to give the homologous methyl ester (LXIII) in good yield. Hydrolysis of this with methanolic potassium hydroxide produced the corresponding propionic acid (LXIV).



(LXIII)



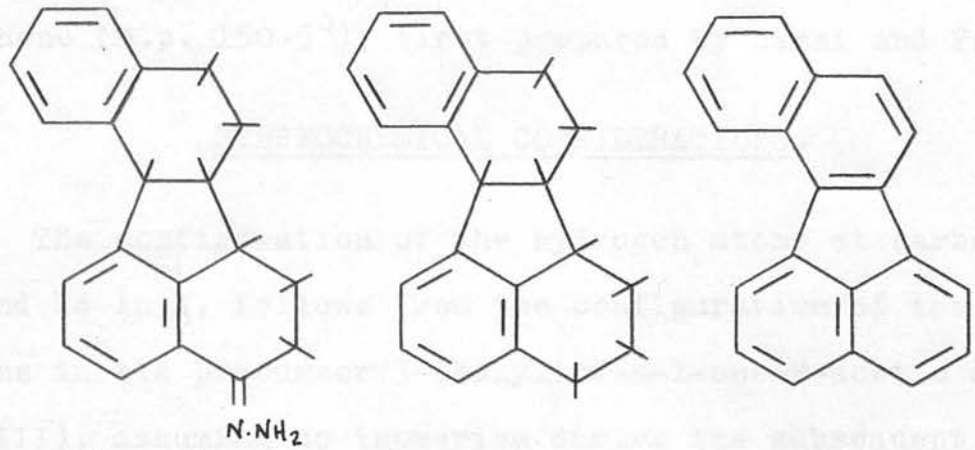
(LXIV)



(LXV)

Ring closure of the propionic acid proved difficult. Attempts to prepare the cyclic ketone (LXV) by cyclising with liquid hydrogen fluoride failed. Cyclisation was effected using the inverse Friedel-Crafts reaction (24), and a 70% yield of the cyclic ketone (LXV) was obtained by treating a solution of the acid chloride of (LXIV) in

sym-tetrachloroethane with stannic chloride.



(LXVI) (A) (II)

Treatment of the ketone (LXV) with excess hydrazine hydrate produced the corresponding hydrazone (LXVI), and this on reduction with ethylene glycol-potassium hydroxide gave the octahydro-10,11-benzfluoranthene (A) as colourless needles (m.p. 150°). Dehydrogenation of (A), by heating with tetrachloro-o-quinone in benzene, produced 10,11-benzfluoranthene (II) as yellow needles (m.p. 163-5°, picrate m.p. 193-5°).

SUMMARY.

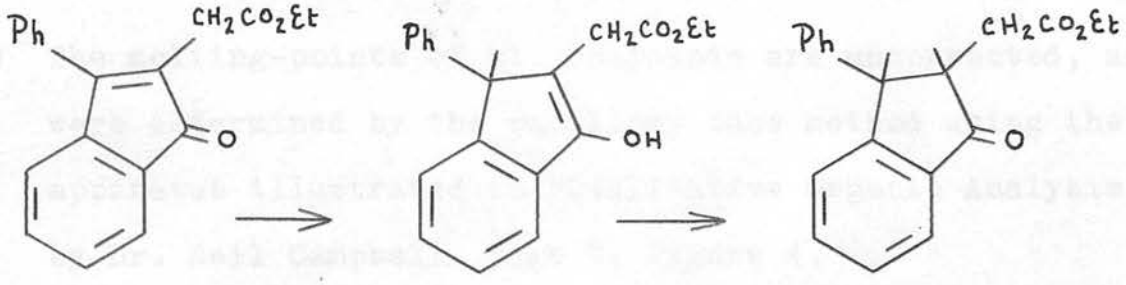
The results of this work fully substantiate Nenitzescu's structure A for 1,2,3,4,9,12,13,14-octahydro-10,11-benzfluoranthene (m.p. 150·5°), first prepared by Dansi and Ferri (2).

STEREOCHEMICAL CONSIDERATIONS.

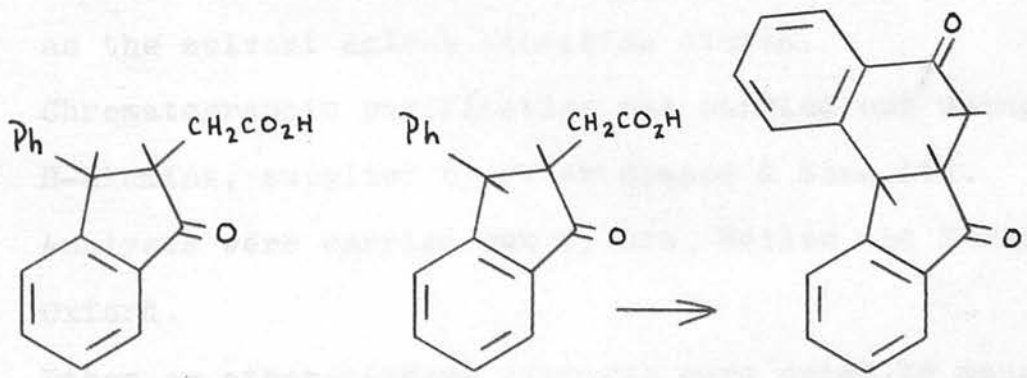
The configuration of the hydrogen atoms at carbon atoms 9 and 14 in A, follows from the configuration of the hydrogen atoms in its precursor 3-phenylindan-1-one-2-acetic acid (XXIII), assuming no isomerism during the subsequent stages of the synthesis.

It is known that cis addition is involved in the catalytic hydrogenation of ethylenic bonds (28), but as pointed out in a more recent review (29), addition is not always exclusively cis, the ultimate configuration depending upon the type of catalyst, temperature and pressure of reaction, solvent, and stereochemistry of substrate.

One further factor in the hydrogenation of (XXI), which would give rise to a trans product, might arise by initial hydrogenation to an enol (1,4-addition), followed by ketonisation (30).



This possibility of enolisation or trans isomer formation was not rigorously examined. A study of the molecular model reveals that although the cis acid (XXIII) would undergo ring closure most easily, cyclisation of the trans isomer is not precluded. This, however, would introduce severe strain into the molecule, and render the formation of the trans diketone (XXIV) unlikely.



XXIII XXIV

On the basis of these arguments, the most stable structure of (XXIV), and hence A, is that in which the hydrogen atoms at 4 and 9 (9 and 14) are cis.

INTRODUCTION TO EXPERIMENTAL

(1) The melting-points of all compounds are uncorrected, and were determined by the capillary tube method using the apparatus illustrated in "Qualitative Organic Analysis" by Dr. Neil Campbell, page 7, figure 4.

(2) Infrared spectra were determined using a Perkin-Elmer Infrared Spectrophotometer. The intensity of absorption maxima are indicated by strong(s), medium(m), and weak(w). The group corresponding to the particular absorption maxima is written below the absorption wave number.

(3) Ultraviolet spectra were determined using a Unicam S.P. 500 Spectrophotometer. Spectroscopic ethanol was used as the solvent unless otherwise stated.

(4) Chromatographic purification was carried out using type H-alumina, supplied by Peter Spence & Sons Ltd.

(5) Analyses were carried out by Drs. Weiler and Strauss, Oxford.

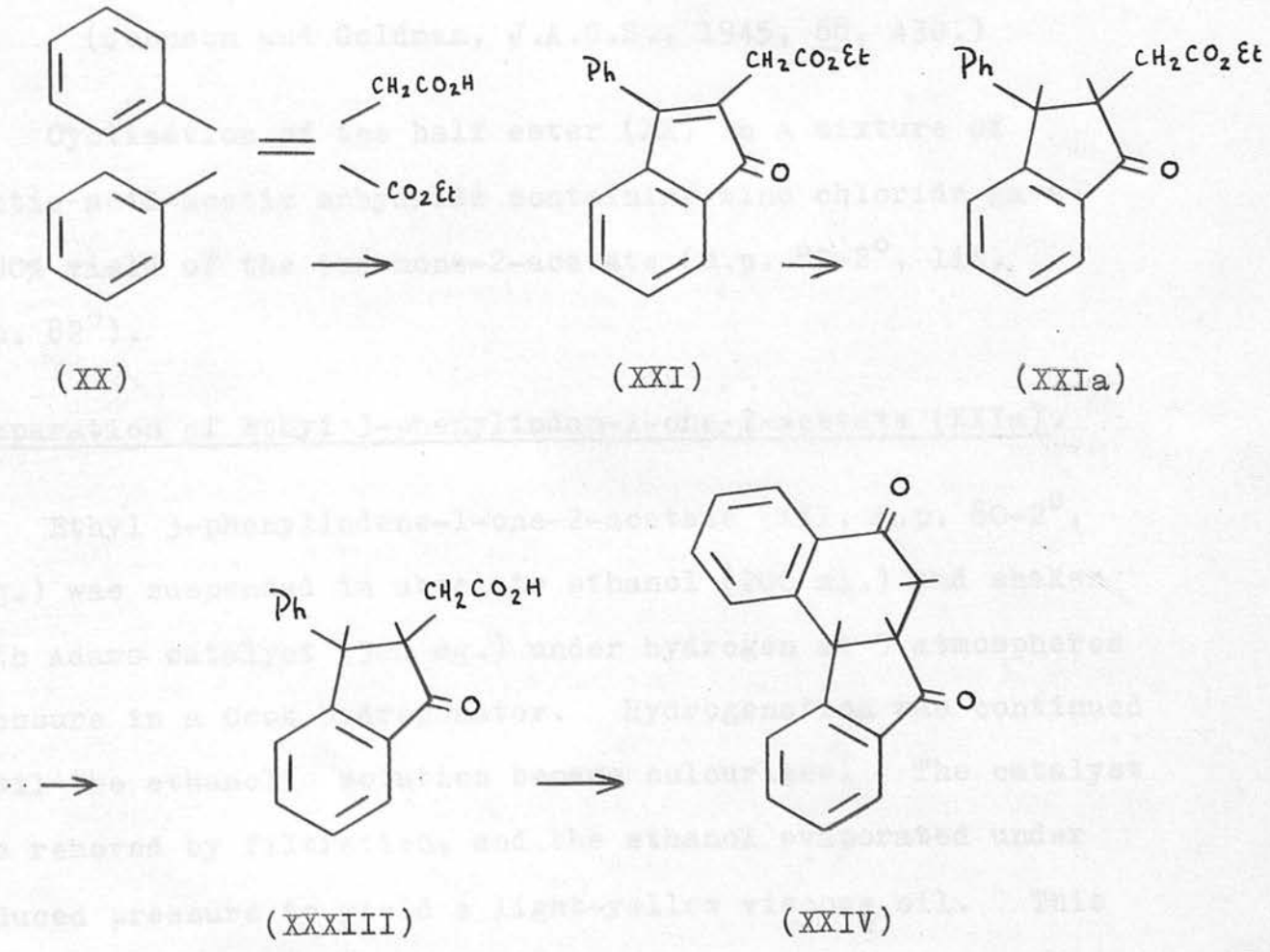
(6) Ether or ether-benzene extracts were dried by means of anhydrous sodium sulphate.

EXPERIMENTAL PART I

SECTION A

The Synthesis of 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2,9-dione (XXIV).

SCHEME A



(XX) (XXI) (XXIa)

(XXXIII) (XXIV)

Preparation of β-carbethoxy-γ,γ-diphenylvinylacetic acid (XX).

(Johnson et al., J.A.C.S., 1946, 69, 74.)

The Stobbé reaction on benzophenone in potassium-tert-butoxide gave an 85% yield of the half ester (m.p. 124-6°, lit. m.p. 124·5-5·5°).

Preparation of Ethyl 3-phenylindene-1-one-2-acetate (XXI).

(Johnson and Goldman, J.A.C.S., 1945, 68, 430.)

Cyclisation of the half ester (XX) in a mixture of acetic acid-acetic anhydride containing zinc chloride gave a 90% yield of the indenone-2-acetate (m.p. 80-2°, lit. m.p. 82°).

Preparation of Ethyl 3-phenylindan-1-one-2-acetate (XXIa).

Ethyl 3-phenylindene-1-one-2-acetate (XXI, m.p. 80-2°, 40g.) was suspended in absolute ethanol (200 ml.) and shaken with Adams catalyst (500 mg.) under hydrogen at 5 atmospheres pressure in a Cook hydrogenator. Hydrogenation was continued until the ethanolic solution became colourless. The catalyst was removed by filtration, and the ethanol evaporated under reduced pressure to yield a light-yellow viscous oil. This was dissolved in petrol (40/60°, 200 ml.), allowed to cool

slowly, whereupon the product crystallised from the solution as needles (m.p. 50-2°). Two further recrystallisations from the same solvent gave ethyl 3-phenylindan-1-one-2-acetate (XXIa), as colourless prismatic needles (m.p. 58-9°, 35g.)

Analysis

$C_{19}H_{18}O_3$ requires C, 77·53; H, 6·16%

found C, 77·77; H, 6·12%

Infrared spectrum (cm^{-1})

1740 (s) 1720 (s)

(ester C=O) (5-ring C=O).

Preparation of 3-phenylindan-1-one-2-acetic acid (XXIII).

The indanone-2-acetic ester (m.p. 58-9°, 35g.) in ethanol (150 ml.) was boiled under reflux with potassium hydroxide (20g.) in water (30 ml.) for two hours. The condenser was set for distillation and ethanol (100 ml.) distilled off, with simultaneous addition of an equivalent volume of water. The solution was diluted with water (250 ml.) and extracted with ether. The aqueous alkaline phase was acidified with hydrochloric acid, and a white granular solid precipitated from the solution. The dry crude acid (m.p. 118-24°) was recrystallised from dilute acetic acid to give 3-phenylindan-1-one-2-acetic acid, as colourless needles (m.p. 130-2°, 28g. lit. m.p. 131-3°).

Infrared spectrum (cm^{-1}.)

1745 (s)	1710 (s)	1240 (m)
(C=O sat. acid)	(5-ring C=O)	(CO_2H)

This acid was shown to be identical to that prepared by Koelsch (12) from the cyclisation of β-benzoyl-β-benzilidenepropionic acid.

Preparation of 1,2,4a,9a-Tetrahydro-3,4-benzfluorene-2,9-dione (XXIV).

(a) Polyphosphoric Acid Cyclisation:

3-Phenylindan-1-one-2-acetic acid (m.p. 130-2°, 1g.) was added to polyphosphoric acid (20 ml.) and the mixture heated at 95° for 45 minutes. During this time the mixture developed a green fluorescence. The reaction mixture was then poured upon ice, and the grey precipitate extracted into benzene-ether (1:1). The ethereal solution was washed with water, sodium bicarbonate solution (5%). Acidification of the alkaline extract with hydrochloric acid precipitated a white solid, which crystallised from dilute acetic acid, to give the unchanged acid (m.p. 130-2°, 350 mg.).

Evaporation of the dried ethereal solution produced an orange solid which crystallised from ethanol to give 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2,9-dione, as long colourless prismatic needles (m.p. 165-7°, 300 mg.).

Analysis

$C_{17}H_{12}O_2$ requires C, 82·24; H, 4·87%

found C, 82·40; H, 4·90%

Infrared spectrum (cm^{-1}.)

1715 (S) 1685 (S)

(5-ring C=O) (6-ring C=O).

(b) Sulphuric Acid Cyclisation:

(Koelsch, J. org.Chem., 1961, 2590.)

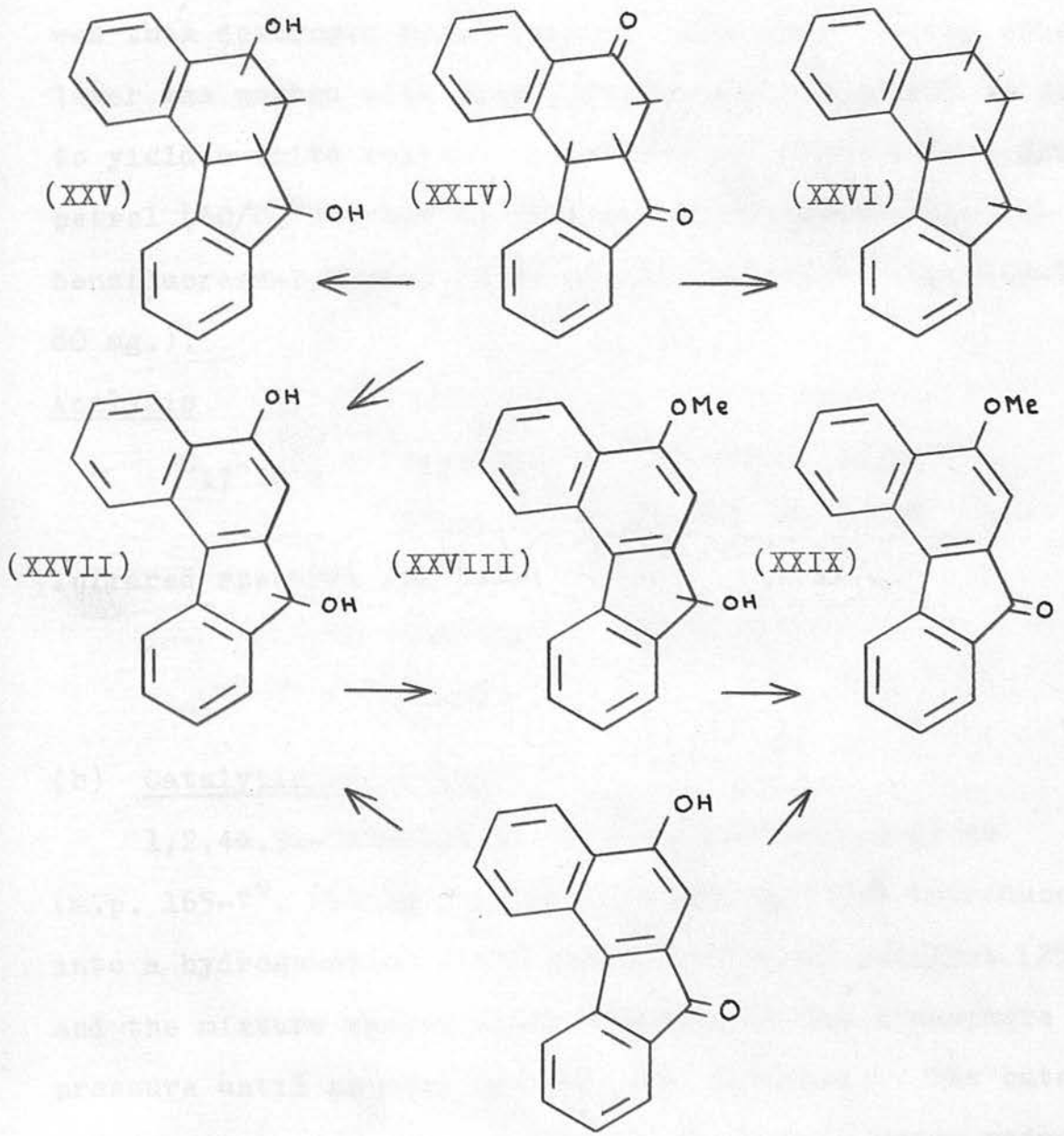
3-Phenylindan-1-one-2-acetic acid (m.p. 130-2°, 1·2g.) was dissolved in concentrated sulphuric acid (6 ml.) and heated at 100° during four minutes. The dark-green solution was then poured upon ice, and the pink precipitate taken into ether. The acidic fraction was removed by washing with sodium bicarbonate solution (5%), and this on acidification with hydrochloric acid, gave a white solid which crystallised from dilute acetic acid as colourless needles (m.p. 130-1°, 150 mg.). This material did not depress the melting-point of a specimen of 3-phenylindan-1-one-2-acetic acid.

The neutral ethereal solution was evaporated to dryness yielding an orange solid. This material was dissolved in benzene, and filtered through a short column of alumina. Elution with the same solvent gave a colourless solid which crystallised from ethanol to give 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2,9-dione (m.p. and mixed m.p. 165-7°, 350 mg.).

SECTION B

Reduction of the diketone (XXIV) and oxidation of the diol (XXV).

SCHEME B.



(XXII)

Reduction of the Diketone (XXIV).

(a) Lithium Aluminium Hydride:

1,2,4a,9a-Tetrahydro-3,4-benzfluorene-2,9-dione (m.p. 165-7°, 100 mg.) was dissolved in anhydrous ether (75 ml.) and treated with lithium aluminium hydride (75 mg.). The mixture was refluxed for one hour, and excess reagent was then destroyed by addition of iced-water. The ethereal layer was washed with water, dried, and evaporated to dryness to yield a white solid. This material crystallised from petrol (60/80°)-ether to give 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2,9-diol (XXV) as silky needles (m.p. 169-70°, 80 mg.).

Analysis

$C_{17}H_{16}O_2$ requires C, 80·92; H, 6·39%

found C, 80·96; H, 6·21%

Infrared spectrum (cm^{-1}.)

3350 (m)

(OH)

(b) Catalytic Reduction:

1,2,4a,9a-Tetrahydro-3,4-benzfluorene-2,9-dione (m.p. 165-7°, 250 mg.) in ethanol (75 ml.) was introduced into a hydrogenation flask containing Adams catalyst (25 mg.) and the mixture shaken under hydrogen at one atmosphere pressure until no more hydrogen was absorbed. The catalyst was filtered off, and the ethanol evaporated under reduced

pressure to yield a colourless oil. This was dissolved in petrol (60/80°)-benzene (1:1, 50 ml.), filtered through a short column of alumina, and the following fractions separated:-

(i) Elution with petrol (60/80°)-benzene (3:1, 150 ml.) gave after evaporation of the solvent, a colourless oil (150 mg.). This material solidified on trituration with petrol (40/60°), and crystallised from petrol (60/80°) to give 1,2,4a,9a-tetrahydro-3,4-benzfluorene (XXVI) as silky colourless needles (m.p. 178-9°, 120 mg.).

Analysis

$C_{17}H_{16}$	requires	C, 92·68;	H, 7·32%
	found	C, 92·79;	H, 7·13%

The infrared spectrum indicates the absence of hydroxyl or carbonyl groups.

(ii) Elution with benzene-ether (4:1, 100 ml.) yielded a colourless solid (50 mg.). This was recrystallised from petrol (60/80°) as silky needles (m.p. 168-70°), undepressed on admixture with 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2,9-diol (XXV).

Chromic Oxide-Pyridine[22] oxidation of the diol (XXV):

A solution of the diol (m.p. 168-70°, 250 mg.) in dry pyridine (10 ml.) was added to a slurry of chromic oxide (500 mg.) in dry pyridine (10 ml.) and the mixture

allowed to stand at room temperature for 16 hours. The pyridine liquor was diluted with water, and the complex destroyed by addition of a slight excess of dilute sodium hydroxide solution. The deep-blue alkaline solution was extracted with ether, and the ether extract washed with hydrochloric acid (5%), water, dried and evaporated to yield a yellow gum. Chromatographic purification on alumina by eluting with petrol (60/80°)-benzene (1:2, 150 ml.), gave a light-yellow oil (180 mg.) which crystallised from petrol (60/80°)-benzene to give 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2,9-dione (XXIV) as colourless needles (m.p. 165-7°, 150 mg.).

The aqueous alkaline fraction was acidified with hydrochloric acid, and extracted with ether. The ethereal solution was washed with water, dried, and evaporated to dryness. The residual red oil crystallised from benzene to give (XXVII) as pink needles (m.p. 234-8°, 25 mg.). The infrared spectrum of this material showed hydroxyl but no carbonyl absorption.

Preparation of 3,4-Benzfluorene-2,9-diol (XXVII).

The diketone (XXIV, m.p. 165-7°, 500 mg.) was dissolved in methanol (20 ml.) and treated with sodium hydroxide (1·5g.) in water(5 ml.). The solution was refluxed for 5 minutes, developing a deep-blue colouration. Dilution

with water followed by acidification with hydrochloric acid precipitated a pink solid. This was filtered off, washed with water, dried and crystallised from benzene as pale pink needles (m.p. 236-40°). Two further recrystallisations from the same solvent gave 3,4-benzfluorene-2,9-diol as almost colourless needles (m.p. 249-51°, 350 mg.).

Analysis

$C_{17}H_{12}O_2$	requires	C, 82·24;	H, 4·87%
	found	C, 81·54;	H, 4·90%

Infrared spectrum (cm^{-1}.)

3,400 (m)

(OH)

The spectrum in hexachlorobutadiene shows no CH_2 absorption.

Preparation of 2-Methoxy-3,4-benzfluorene-9-ol (XXVIII).

3,4-Benzfluorene-2,9-diol (XXVII, m.p. 247-9°, 250 mg.) was dissolved in warm sodium hydroxide solution (20 ml., 2N). The solution became dark blue, and on cooling a small amount of blue solid precipitated out. This was dissolved by addition of methanol (10 ml.) and dimethyl sulphate (10 ml.) added portionwise with shaking, until the blue colour disappeared completely. The pink solid produced was extracted into ether, and the ether solution washed with water, dried, and evaporated to dryness. The

residual pink solid crystallised from petrol (60/80°)-ether to give 2-methoxy-3,4-benzfluorene-9-ol as pink needles (m.p. 132-6°, 220 mg.). Two further recrystallisations from the same solvent gave pink needles (m.p. 138-40°).

Analysis

$C_{18}H_{14}O_2$ requires C, 82·42; H, 5·38%

found C, 81·61; H, 5·34%

Infrared spectrum (cm^{-1}.)

3,300 (m) (OH) 1265 (s) (OCH_3)

Preparation of 2-Methoxy-3,4-benzfluorene-9-one (XXIX).

A solution of 2-methoxy-3,4-benzfluorene-9-ol (XXVIII, m.p. 138-40°, 150 mg.) in dry pyridine (10 ml.) was added to a slurry of chromic oxide (500 mg.) in dry pyridine (10 ml.) and the mixture allowed to stand at room temperature for 16 hours. The reaction mixture was diluted with water, and rendered alkaline by addition of a slight excess of 2N sodium hydroxide solution. The ether soluble material was washed with hydrochloric acid (5%), water, dried and evaporated to dryness to yield a deep-red solid, melting-point in the region of 150°. Three crystallisations from acetone-petrol (60/80°) gave 2-methoxy-3,4-benzfluorene-9-one as red needles (m.p. 155-7°, 100 mg. lit. m.p. 155-7°).

Analysis

Found: C, 82·2; H, 4·6% Calc. for $C_{18}H_{12}O_2$: C, 83·1; H, 4·65.

Infrared spectrum (cm^{-1}.)

1720 (s) (5-ring C=O) 1270 (s) (OCH_3)

Lithium aluminium hydride reduction of 2-Hydroxy-3,4-benzfluorene-9-one (XXII).

2-Hydroxy-3,4-benzfluorene-9-one (m.p. 259-61°, 100 mg.) was dissolved in anhydrous ether (100 ml.), and the cold solution treated with lithium aluminium hydride (100 mg.). After the initial reaction had subsided, the reaction mixture was refluxed for 1 hour. Excess reagent was destroyed by cautious addition of iced-water, and the ethereal layer was separated from the lithium and aluminium hydroxides by decantation, washed with water, dried and evaporated to dryness. The residual white solid gave, after three recrystallisations from benzene, colourless needles (m.p. 248-50°, 80 mg.). This material caused no depression of the melting-point on admixture with a specimen of 3,4-benzfluorene-2,9-diol (XXVII). The infrared spectra are identical.

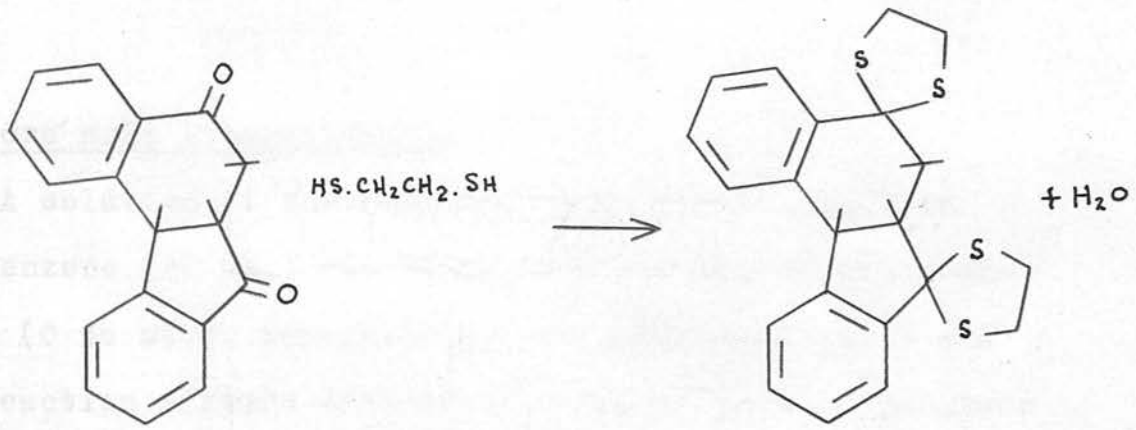
Methylation of 2-Hydroxy-3,4-benzfluorene-9-one (XXII).

2-Hydroxy-3,4-benzfluorene-9-one (m.p. 259-61°, 100 mg.) was dissolved in 2N sodium hydroxide solution (20 ml.) and dimethyl sulphate (10 ml.) added portionwise with shaking until the blue colour disappeared completely. The red precipitate was extracted into ether, and the ether solution washed with water, dried and evaporated to dryness to give a red solid. Recrystallisation from acetone-petrol (60/80°) gave 2-methoxy-3,4-benzfluorene-9-one (XXIX) as red needles (m.p. 155-7°, 75 mg.). This material showed an infrared spectrum identical to, and did not depress the melting-point on admixture with, the product of chromic oxide-pyridine oxidation of 2-methoxy-3,4-benzfluorene-9-ol (XXVIII).

SECTION C

Thioketal Formation

(a)



(XXIV) (XXXII)

A solution of the diketone (m.p. 165-7°, 1g.) in dry benzene (30 ml.) was added to a mixture of ethanedithiol (1 ml.), borontrifluoride etherate (3 ml.) and the reaction mixture allowed to stand at room temperature for 16 hours. After this time, the light-brown solution was heated at 45° for 15 minutes, then poured into ether-benzene (1:1, 300 ml.). The ether-benzene extract was thoroughly washed with 2N sodium hydroxide solution, water, dried and evaporated to dryness to give a white solid (m.p. 200-5°, 1·5g.). This was recrystallised twice from ethanol-chloroform to give 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2,9-bis-(dithioketal), (m.p. 216-8°, 1·3g.)

Analysis

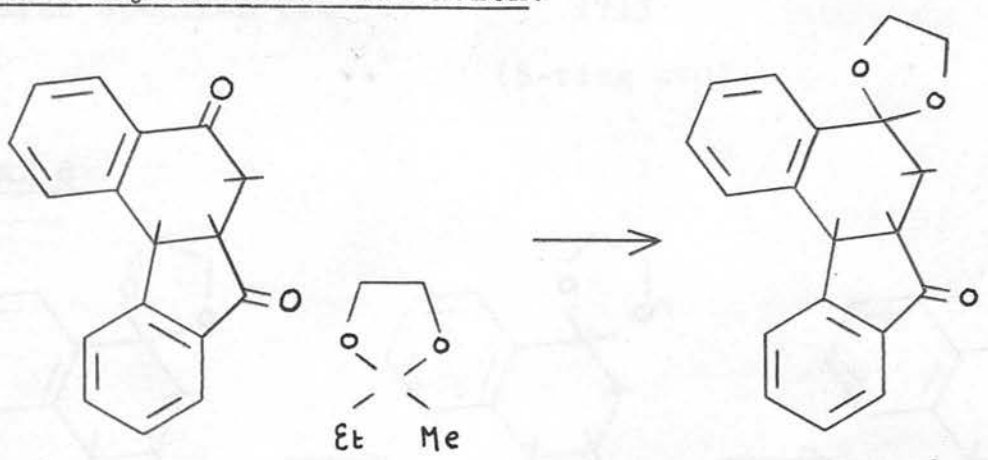
$C_{21}H_{20}S_4$	requires	S, 32·10%
	found	S, 32·80%

The Infrared spectrum shows no carbonyl absorption band.

(b) One Mole Ethanedithiol:

A solution of the diketone (m.p. 165-7°, 1g.) in dry benzene (30 ml.) was added to a mixture of ethanedithiol (0·35 ml.), borontrifluoride etherate (3 ml.) and the reaction mixture allowed to stand at room temperature for 16 hours. The light-brown solution was poured into ether-benzene (1:1, 300 ml.), washed thoroughly with 2N sodium hydroxide solution, water, then dried and evaporated to dryness to give a white solid. This was triturated with hot benzene (30 ml.), filtered, and the residue crystallised from ethanol-chloroform to give colourless prisms (m.p. 207-10°). Two further recrystallisations from the same solvent gave 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2,9-bis-(dithioketal) (XXXII, m.p. 216-8°, 450 mg.). The benzene filtrate was reduced in volume, treated with petrol (60/80°) to give colourless needles (m.p. 155-9°). Two further recrystallisations from the same solvent gave the unchanged diketone (XXIV) as needles (m.p. and mixed m.p. 164-6°, 300 mg.).

Ethylene Glycol Ketal Formation:



(XXIV) (XXXIII)

A mixture of the diketone (m.p. 165-7°, 2g.), p-toluene sulphonic acid monohydrate (50 mg.), was dissolved in 2-methyl-2-ethyl-1,3-dioxolane (22 ml.) and the solution refluxed under anhydrous conditions for four hours. Upon cooling, the reaction mixture was diluted with benzene (250 ml.), washed with 5% sodium bicarbonate solution, water dried and evaporated to dryness under reduced pressure. The residual red solid was dissolved in dry benzene and filtered through a short column of alumina. Elution with the same solvent followed by evaporation of the benzene eluates (300 ml.) gave a white solid (m.p. 190-5°), and this after two recrystallisations from petrol (60/80°)-benzene gave 1,2,4a,9a-tetrahydro-2-ethylenedioxy-3,4-benzfluorene-9-one (XXXIII) as colourless needles (m.p. 199-201°, 2g.).

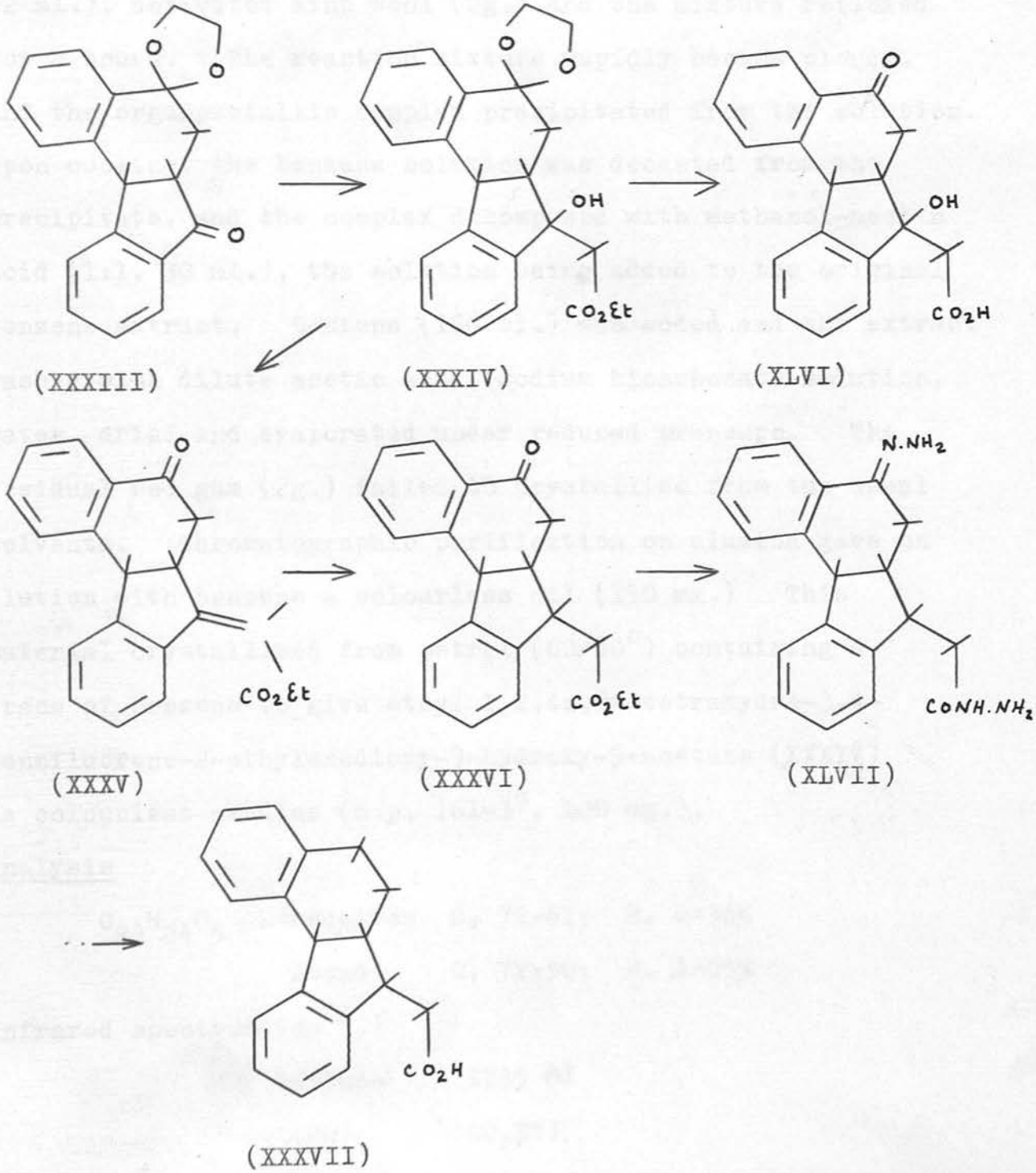
Analysis

$C_{19}H_{16}O_3$	requires	C, 78·06;	H, 5·52%
	found	C, 78·10;	H, 5·63%

Infrared spectrum (cm^{-1}.) 1715

(5-ring C=O)

SCHEME C



(XXXIII) (XXXIV) (XLVI)

(XXXV) (XXXVI) (XLVII)

(XXXVII)

The Reformatsky Reaction on the Dioxolane ketone (XXIV).

A solution of the dioxolane ketone (m.p. 196-8°, 2g.) in dry benzene (50 ml.) was treated with ethyl bromoacetate (2 ml.), activated zinc wool (2g.) and the mixture refluxed for 2 hours. The reaction mixture rapidly became cloudy, and the organometallic complex precipitated from the solution. Upon cooling, the benzene solution was decanted from the precipitate, and the complex decomposed with methanol-acetic acid (1:1, 30 ml.), the solution being added to the original benzene extract. Benzene (150 ml.) was added and the extract washed with dilute acetic acid, sodium bicarbonate solution, water, dried and evaporated under reduced pressure. The residual red gum (2g.) failed to crystallise from the usual solvents. Chromatographic purification on alumina gave on elution with benzene a colourless oil (150 mg.) This material crystallised from petrol (60/80°) containing a trace of benzene to give ethyl 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2-ethylenedioxy-9-hydroxy-9-acetate (XXXIV) as colourless needles (m.p. 161-3°, 100 mg.).

Analysis

$C_{23}H_{24}O_5$	requires	C, 72·61; H, 6·36%
	found	C, 72·50; H, 6·05%

Infrared spectrum (cm^{-1}.)

3550 (m)	1735 (s)
(OH)	(CO_2Et)

The major portion of the product, an uncrystallisable red oil (1·5g.), was obtained on 'stripping' the column with ether-methanol (5%). Portions of this material were subjected to acid dehydration and alkaline hydrolysis.

Dehydration of the Reformatsky Product:

The red oil (500 mg.) was dissolved in formic acid (90%, 20 ml.) heated at 100° for 45 minutes, and then allowed to stand at room temperature for 4 hours. Dilution with water (30 ml.) followed by evaporation under reduced pressure, gave a residual dark-red gum, which was dissolved in ether. The ethereal solution was washed with sodium bicarbonate solution (5%), water, dried and evaporated to dryness. The residual red gum was dissolved in petrol (60/80°)-benzene (2:1, 50 ml.) and filtered through a short column of alumina (10g.). Elution with benzene-ether (9:1) gave a small amount of a yellow oil, which crystallised from benzene as plates (m.p. 144-6°). Two recrystallisations from the same solvent gave the keto-unsaturated ester (XXXV) as colourless blades (m.p. 148-50°, 50 mg.).

Analysis

$C_{21}H_{18}O_3$	requires	C, 79·22;	H, 5·70%
	found	C, 80·00;	H, 5·76%

Infrared spectrum (cm^{-1}.)

1705 (s)	1680 (s)	1650 (m)
(α,β-unsatd.CO_2Et)	(6-ring C=O)	(C=C)

The major product, a viscous red gum, obtained on 'stripping' the column with ether-methanol (5%), did not crystallise, and was not further investigated.

Alkaline Hydrolysis of the Reformatsky Product:

The red oil (1·0g.) was dissolved in ethanol (15 ml.) and boiled under reflux with potassium hydroxide (3g.) in water (12 ml.) for 2 hours. Ethanol (10 ml.) was distilled off, with simultaneous addition of water (15 ml.). The solution was diluted with water (100 ml.), extracted with ether, and the neutral ethereal extract removed. The aqueous alkaline phase was acidified with hydrochloric acid, and a pink crystalline solid precipitated from the solution on standing. This material was filtered off, washed with water and dried. The crude acid (m.p. 194° decomp.) was triturated with hot ethanol (15 ml.) and the suspension filtered. Upon cooling, the ethanol deposited 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2-one-9-hydroxy-9-acetic acid (XLVI) as fine silky needles (m.p. 214° decomp., 100 mg.).

Analysis

$C_{19}H_{16}O_4$	requires	C, 74·01; H, 5·23%
	found	C, 74·38; H, 5·13%

Infrared spectrum (cm^{-1}.)

3450 (m)	1700 (s)	1675 (s)
(OH)	(CO_2H)	(6-ring C=O).

The major portion of the product (500 mg.), the alcohol insoluble material, was recrystallised from acetic acid to give colourless prisms (m. p. 207° decomp.). The structure of this material has not been established.

Preparation of the saturated ester (XXXVI).

A solution of the unsaturated ester (XXXV, m.p. 144-6°, 400 mg.) in ethyl acetate (50 ml.) was added to a suspension of Adams catalyst (50 mg.) in ethyl acetate (25 ml.), and the mixture shaken in an atmosphere of hydrogen, until the theoretical amount of hydrogen had been taken up (2 hours). The catalyst was filtered off, and the ethanol removed under reduced pressure. The residual colourless oil was filtered through a short column of alumina (10g.) in benzene. Evaporation of the eluate followed by crystallisation of the residual oil from petrol (60/80°) gave colourless prisms (m.p. 85-8°). Two further recrystallisations from the same solvent gave ethyl 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2-one-9-acetate (XXXVI) as prisms (m.p. 94-6°, 275 mg.).

Analysis

$C_{21}H_{20}O_3$	requires	C, 78·72;	H, 6·29%
	found	C, 78·11;	H, 6·20%

Infrared spectrum (cm^{-1}.)

1735 (s)	1680 (s)
(satd.CO_2Et)	(6-ring C=O)

Preparation of the Hydrazone hydrazide (XLVII):

A solution of the saturated ester (XXXVI, m.p. 92-4°, 80 mg.) in ethanol (5 ml.) was treated with hydrazine hydrate (99%, 1 ml.) and the mixture heated on the steam-bath for 10 minutes. Upon cooling, the hydrazone hydrazide (XLVII) crystallised out as colourless rosettes (m.p. 252-4°, 50 mg.).

Infrared spectrum (cm^{-1}.) 3350, 3200 (m) (NH_2) 1650 (s) (CONH)

Wolff-Kishner reduction of the Hydrazone hydrazide:

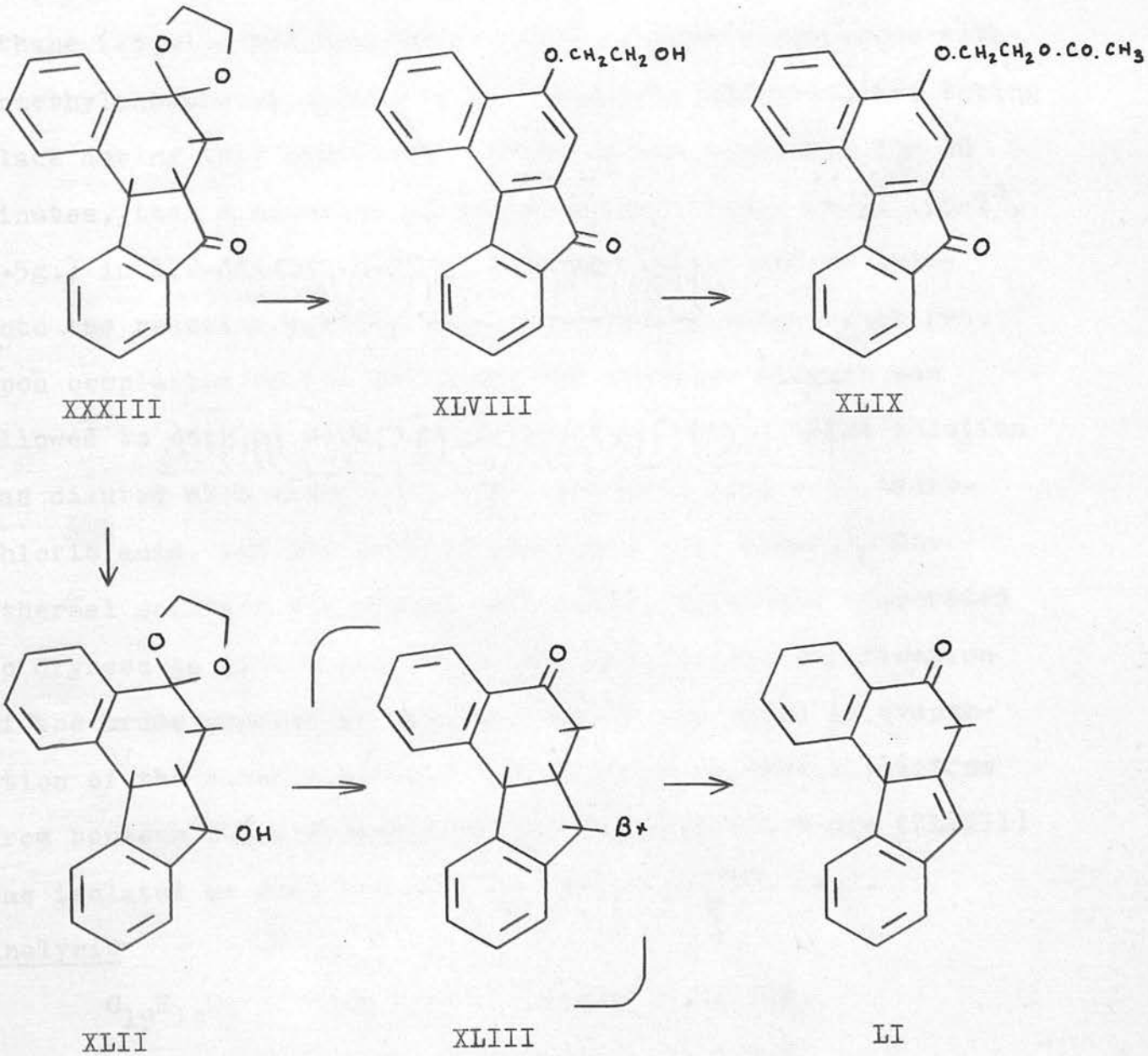
The hydrazone hydrazide (m.p. 252-4°, 50 mg.) was suspended in ethylene glycol (25 ml.) containing potassium hydroxide (1g.) and the mixture refluxed for 2 hours. Ethylene glycol (6 ml.) was removed, and reflux maintained for a further 2 hours. The cold solution was diluted with water (50 ml.) acidified with hydrochloric acid and the white precipitate extracted into ether. The ethereal solution was washed with water, then with sodium bicarbonate solution. Acidification of the bicarbonate extract with hydrochloric acid precipitated a white solid. This was filtered off, washed with water, dried and crystallised from petrol (60/80°)-benzene as colourless prisms (m.p. 216-8°, 20 mg.).

Infrared spectrum (cm^{-1}.) 1720 (s) (C=O, satd. acid) 1240 (m) (CO_2H)

This material proved to be identical with (XXVII) described in a later part of this work.

SECTION D

SCHEME D.



XXXIII XLVIII XLIX

XLII XLIII LI

The Modified Wittig Reaction on the Dioxolane ketone (XXXIII)[17].

A stirred suspension of sodium hydride (50% dispersion in mineral oil, 1g.) in anhydrous 1,2-dimethoxyethane (25 ml.) was treated dropwise at room temperature with triethylphosphonoacetate (5g.), a vigorous effervescence taking place during this addition. Stirring was continued for 30 minutes, then a solution of the dioxolane ketone (m.p. 195-7°, 2·5g.) in 1,2-dimethoxyethane (30 ml.) introduced dropwise into the reaction mixture which immediately became dark red. Upon completion of the addition, the reaction mixture was allowed to stir at room temperature for 1 hour. The solution was diluted with water (200 ml.), rendered acid with hydrochloric acid, and the product extracted into ether. The ethereal solution was washed with water, dried and evaporated to dryness to give a red gum. Chromatographic purification of the crude product on alumina, gave a red solid on evaporation of the ether eluates. After three recrystallisations from benzene 2-β-hydroxyethoxy-3,4-benzfluorene-9-one (XLVIII) was isolated as deep red needles (m.p. 169-71°, 2g.).

Analysis

$C_{19}H_{14}O_3$	requires	C, 78·60;	H, 4·85%
	found	C, 78·71;	H, 4·76%

Molecular Weight 291, theoretical 290·3.

Infrared spectrum (cm^{-1}.)

3450 (m)	1705 (s)	1580 (m)
(OH)	(5-ring C=O)	(aromatic ring)

Preparation of 2-β-acetylethoxy-3,4-benzfluorene-9-one (XLIX):

2-β-hydroxyethoxy-3,4-benzfluorene-9-one (XLVIII, m.p. 169-71°, 150 mg.) was dissolved in glacial acetic acid-acetic anhydride mixture (1:1, 15 ml.), concentrated sulphuric acid (1 drop) added, and the mixture heated at 90° for 15 minutes. Upon cooling, the solution was diluted with water (50 ml.) and a red solid precipitated from the solution. This was filtered off, washed with water and dried. Three recrystallisations from petrol (60/80°) gave 2-β-acetylethoxy-3,4-benzfluorene-9-one (XLIX) as long red needles (m.p. 136-8°, 130 mg.)

Analysis

$C_{21}H_{16}O_4$	requires	C, 75·89; H, 4·85%
	found	C, 76·50; H, 4·89%

Infrared spectrum (cm^{-1}.)

1740 (s)	1715 (s)
(acetate C=O)	(5-ring C=O)

The N.M.R. spectrum shows the following ratio of protons:-

9	4	3
aromatic	$O \cdot CH_2CH_2 \cdot O$	$CO \cdot CH_3$

Attempted Stobbé Condensation.

Action of Potassium-tert-butoxide on the keto-dioxolane (XXXIII).

The keto-dioxolane (m.p. 165-7°, 2g.) was introduced into potassium-tert-butoxide from t-butanol (30 ml.) potassium (0·5g.) and the mixture, which immediately became dark red in colour, stirred at 90° for 5 minutes. Upon cooling, the reaction mixture was diluted with water, and acidified with hydrochloric acid. The product was extracted into ether and, washed until neutral with saturated salt solution, water, dried and evaporated under reduced pressure to give a red gum (2g.). This material crystallised from benzene as red needles (m.p. 163-6°). Two further recrystallisations from the same solvent gave red micro-needles (m.p. 169-71°, 1·75g.). This material gave no depression on mixture with a specimen of 2-β-hydroxyethoxy-3,4-benzfluorene-9-one (XLVIII). The infrared spectra are identical.

Preparation of 1,2,4a,9a-tetrahydro-2-ethylenedioxy-3,4-benzfluorene-9-ol (XLII).

The keto-dioxolane (XXXIII, m.p. 165-7°, 1·0g.) was suspended in ethanol (60 ml.) and refluxed for 2 hours with potassium borohydride (500 mg.). The ethanol was distilled

off and water (150 ml.) added. The white precipitate was dissolved in ether, and the ether extract washed with water, dried and evaporated to dryness to give a colourless oil (1·0g.). This crystallised from petrol (60/80°)-benzene as colourless rosettes (m.p. 112-4°). After two recrystallisations from the same solvent gave 1,2,4a,9a-tetrahydro-2-ethylenedioxy-3,4-benzfluorene-9-ol as silky needles (m.p. 116-8°, 900 mg.).

Analysis

$C_{19}H_{18}O_3$	requires	C, 77·53;	H, 6·16%
	found	C, 77·33;	H, 6·20%

Infrared spectrum (cm^{-1}.)

3400 (s)
(OH)

Attempted Preparation 1,2,4a,9a-tetrahydro-2-ethylenedioxy-9-bromo-3,4-benzfluorene.

The dioxolane alcohol (XLII, m.p. 116-8°, 2g.) was dissolved in sodium dried ether (60 ml.) and treated dropwise with stirring at 0°, with phosphorus tribromide (2·5 ml.) over 5 minutes. The reaction mixture was allowed to stand at room temperature for 30 minutes. The ethereal solution was washed with 5 % sodium bicarbonate solution, water, dried and evaporated to dryness. The residual yellow oil solidified on trituration with petrol (40/60°). Recrystallisation from petrol (60/80°)-benzene gave the unsaturated ketone (LI) as

colourless prisms (m.p. 156-8°, 800 mg.).

Analysis

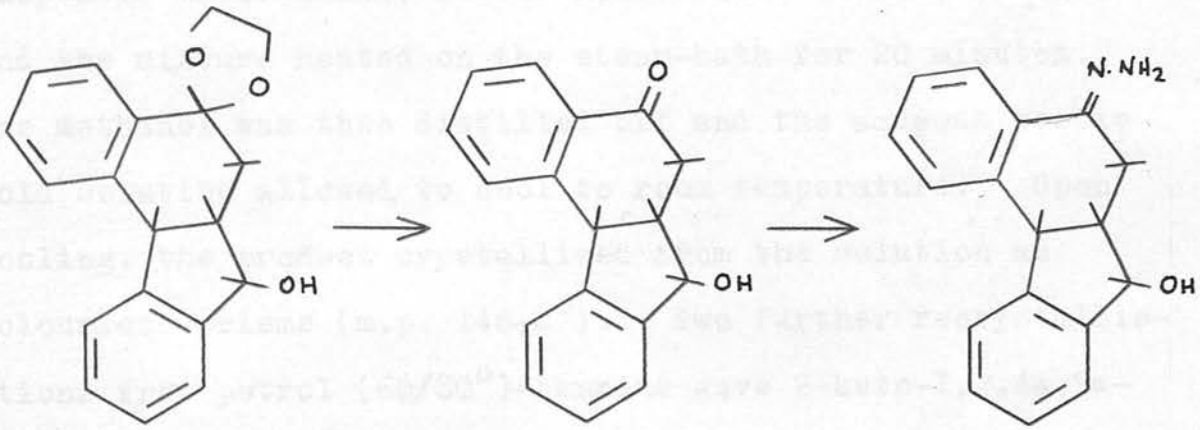
$C_{17}H_{12}O$	requires	C, 87·90; H, 5·21%
	found	C, 87·96; H, 5·25%

Infrared spectrum (cm^{-1}.)

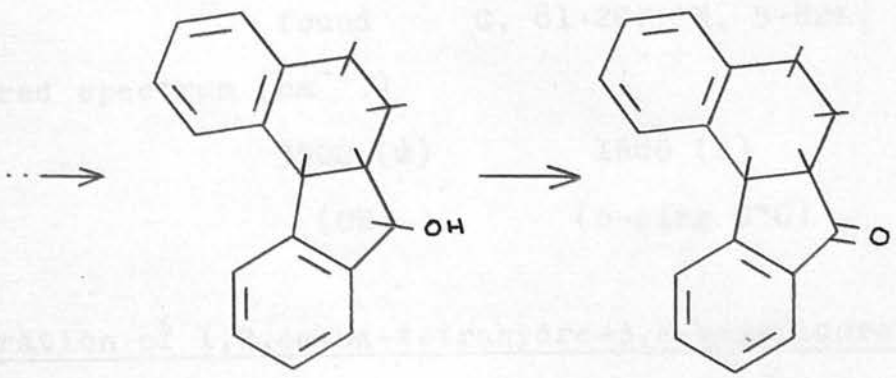
1680 (s)	1625 (s)
(6-ring C=O)	(C=C)

SECTION E.

SCHEME E.



XLII LVIII LIX



LX XXXI

Preparation of 2-keto-1,2,4a,9a-tetrahydro-3,4-benzfluorene-9-ol (LVIII).

The dioxolane alcohol (XLII, m.p. 116-8°, 2g.) was suspended in methanol, acetic acid, water (1:1:1, 45 ml.) and the mixture heated on the steam-bath for 20 minutes. The methanol was then distilled off and the aqueous acetic acid solution allowed to cool to room temperature. Upon cooling, the product crystallised from the solution as colourless prisms (m.p. 146-8°). Two further recrystallisations from petrol (60/80°)-benzene gave 2-keto-1,2,4a,9a-tetrahydro-3,4-benzfluorene-9-ol as colourless prisms (m.p. 150-2°, 1·55g.).

Analysis

$C_{17}H_{14}O_2$	requires	C, 81·58;	H, 5·64%
	found	C, 81·20;	H, 5·82%

Infrared spectrum (cm^{-1}.)

3500 (m)	1680 (s)
(OH)	(6-ring C=O)

Preparation of 1,2,4a,9a-tetrahydro-3,4-benzfluorene-2-one-9-ol hydrazone (LIX).

The ketol (m.p. 150-2° , 1g.) was dissolved in warm absolute ethanol (25 ml.), excess hydrazine hydrate (99%, 2 ml.) added and the solution refluxed gently on steam-bath

for 15 minutes, then allowed to cool. The hydrazone (LIX) crystallised from the solution as colourless needles (m.p. 194-6°, lg.). Recrystallisation from chloroform methanol gave needles (m.p. 196-8°).

Analysis

$C_{17}H_{16}ON_2$	requires	C, 77·25;	H, 6·10;	N, 10·6%
	found	C, 77·00;	H, 5·77;	N, 10·5%

Infrared spectrum (cm^{-1}.)

3400 (w)	3200 (m)	1615 (m)
(OH)	(NH_2)	(C=N).

Wolff-Kishner reduction of the Hydrazone (LIX).

The hydrazone (LIX, m.p. 196-8°, 500 mg.) was dissolved in ethylene glycol (50 ml.) containing potassium hydroxide (2·5 g.) and the mixture refluxed for 2 hours. By means of a modified Dean and Stark separator, ethylene glycol (20 ml.) was removed, and the mixture allowed to reflux for a further 2 hours. Upon cooling, the reaction mixture was diluted with water (120 ml.), and the white precipitate extracted into ether. The ethereal solution was washed thoroughly with water, dried and evaporated to dryness to yield a white solid. Chromatographic purification of this material on alumina produced colourless silky needles (300 mg.) from the benzene-ether (9:1) eluates. Recrystallisation from petrol (60/80°)-benzene gave 1,2,4a,9a-tetrahydro-3,4-

benzfluorene-9-ol (LX) as colourless silky needles (m.p. 166-8°, 275 mg.).

Analysis

$C_{17}H_{16}O$ requires C, 86·40; H, 6·83%

found C, 86·65; H, 6·93%

Infrared spectrum (cm^{-1}.)

3300 (m)

(OH)

Preparation of 1,2,4a,9a-tetrahydro-3,4-benzfluorene-9-one (XXXI).

1,2,4a,9a-Tetrahydro-3,4-benzfluorene-9-ol (LX, m.p. 163-5°, 9·5g.) was dissolved in acetone (200 ml.) cooled in an ice-bath, and treated at 5° with chromic oxide-8N sulphuric acid reagent until the amber chromate colour persisted (15 ml.). The reaction mixture was allowed to stand at 0° for 1 hour then poured into water (600 ml.). The white precipitate was extracted into ether, and the ethereal solution thoroughly washed with water, dried and evaporated to dryness to give a yellow gum (9g.). Chromatographic purification on a short column of alumina, followed by evaporation of the benzene eluate, gave colourless needles (m.p. 109-11°, 8·5g.). Three recrystallisations from petrol (40/60°) gave 1,2,4a, 9a-tetrahydro-10,11-benzfluorene-9-one as colourless

needles (m.p. 116-8°, 7·5g.).

Analysis

$C_{17}H_{14}O$	requires	C, 87·15;	H, 6·02%
	found	C, 87·38;	H, 6·02%

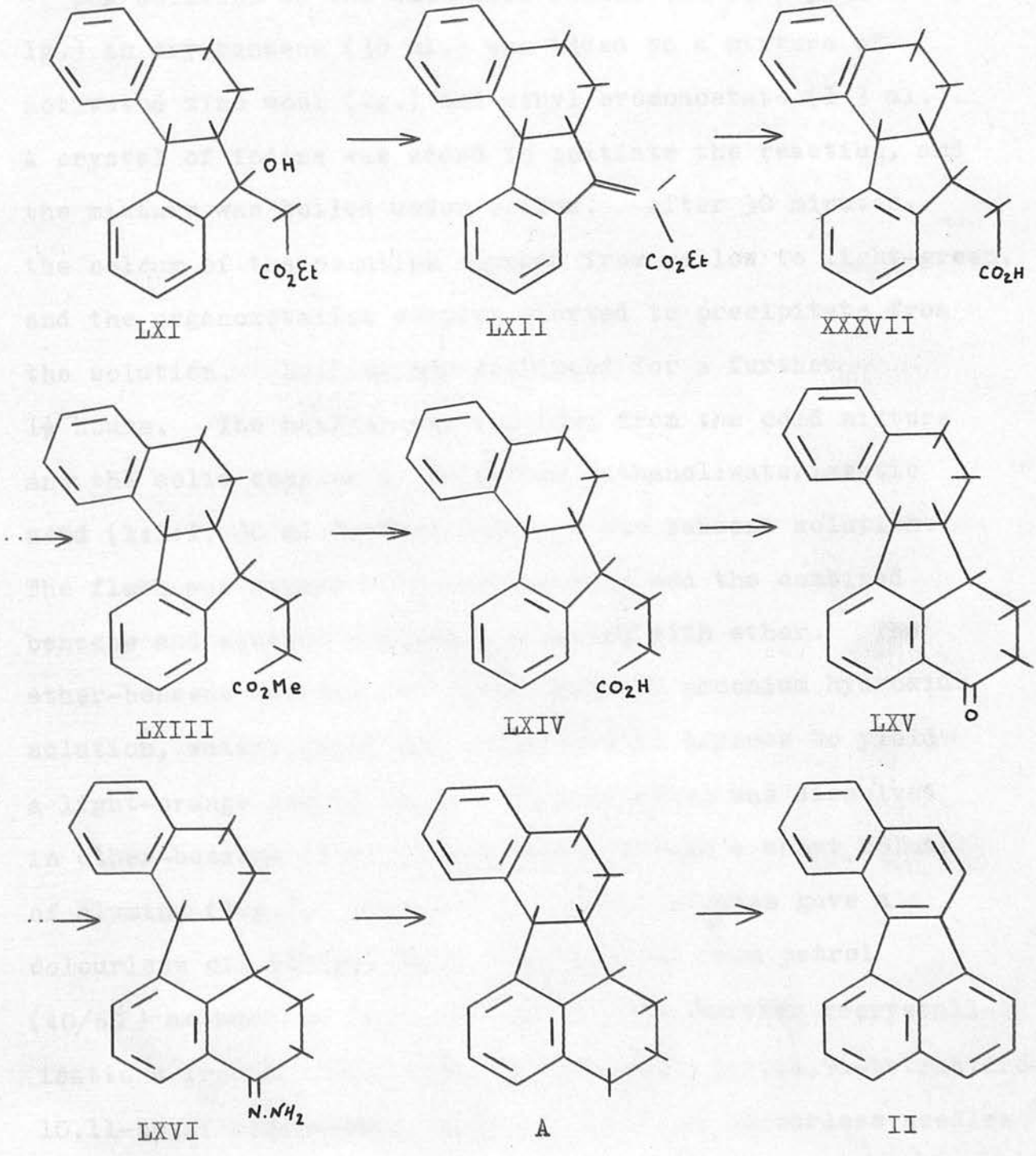
Infrared spectrum (cm^{-1}.)

1715 (s)

(5-ring C=O)

SECTION F.

SCHEME F.



LXI LXII XXXVII

LXIII LXIV LXV

LXVI A II

Preparation of Ethyl 1,2,4a,9a-tetrahydro-3,4-benzfluorene-9-ol-9-acetate (LXI).

A solution of the saturated ketone (XXXI, m.p. 112-4°, 1g.) in dry benzene (30 ml.) was added to a mixture of activated zinc wool (2g.) and ethyl bromoacetate (1·3 ml.). A crystal of iodine was added to initiate the reaction, and the mixture was boiled under reflux. After 30 minutes, the colour of the solution changed from yellow to light-green, and the organometallic complex started to precipitate from the solution. Boiling was continued for a further 1½ hours. The benzene was decanted from the cold mixture and the solid complex dissolved in methanol:water:acetic acid (1:1:1, 30 ml.), then added to the benzene solution. The flask was rinsed with more benzene and the combined benzene and aqueous washings extracted with ether. The ether-benzene extract was washed with 2N ammonium hydroxide solution, water, dried and evaporated to dryness to yield a light-orange gum (1·2g.). This material was dissolved in ether-benzene (1:4) and filtered through a short column of alumina (10g.). Evaporation of the eluates gave a colourless oil (1·1g.) which crystallised from petrol (40/60°) as needles (m.p. 99-103°). Two further recrystallisations from the same solvent gave ethyl 1,2,4a,9a-tetrahydro-10,11-benzfluorene-9-ol-9-acetate (LXI) as colourless needles (m.p. 108-9°, 950 mg.).

Analysis

$C_{21}H_{23}O_3$	requires	C, 78·23;	H, 6·88%
	found	C, 78·58;	H, 6·49%

Infrared spectrum (cm^{-1}.)

3450 (m)	1710 (s)
(OH)	(CO_2Et)

Dehydration of the Reformatsky ester:

(a) 90% Formic acid.

They hydroxy ester (LXI, m.p. 102-4°, 1·4g.) was dissolved in 90% formic acid (20 ml.) and heated at 100° for 2 hours giving an orange solution. The reaction mixture was poured into water (150 ml.) and extracted with ether. The ethereal solution was washed with water, 10% sodium bicarbonate solution, water, dried and evaporated to dryness to give an orange gum. This crystallised from petrol (40/60°) as needles (m.p. 80-2°). Two further recrystallisations from the same solvent gave the α,β-unsaturated ester (LXII) as colourless needles (m.p. 86-8°, 900 mg.).

Analysis

$C_{21}H_{20}O_2$	requires	C, 82·86;	H, 6·62%
	found	C, 82·40;	H, 5·90%

Infrared spectrum (cm^{-1}.)

1720 (s) 1640 (w)

(α,β-unsatd. CO_2Et) (C=C)

(b) Acetic Acid-Hydrochloric Acid:

The hydroxy ester (m.p. 102-4°, 200 mg.) was dissolved in acetic acid (3 ml.), treated with concentrated hydrochloric acid (1 drop) and heated at 100° for 10 minutes giving a red solution. The reaction mixture was poured into water (100 ml.) and extracted with ether. The ethereal solution was thoroughly washed with water, dried and evaporated to dryness to yield a red gum. This material solidified when triturated with petrol (40/60°). Two recrystallisations from the same solvent gave the unsaturated ester (m.p. 82-4°, 140 mg.), undepressed on admixture with a sample of the product from the previous experiment. The infrared spectra are identical.

Preparation of 1,2,4a,9a-tetrahydro-3,4-benzfluorene-9-acetic acid (XXXVII):

A suspension of the unsaturated ester (LXII, m.p. 84-6°, 5g.) in ethanol (100 ml.) was added to a suspension of Adams catalyst (500 mg.) in ethanol (25 ml.) and the mixture shaken under hydrogen until the theoretical amount of hydrogen had been taken up (1½ hours). The catalyst was filtered off and the ethanol evaporated under reduced pressure to give a

colourless oil (5g.). This was dissolved in ethanol (40 ml.) treated with potassium hydroxide (4g.) in water (8 ml.) and the mixture refluxed for 2 hours. The ethanol was distilled off with simultaneous addition of an equivalent volume of water. The solution was diluted with water (100 ml.) and extracted with ether. The aqueous alkaline phase was acidified with hydrochloric acid and a white crystalline solid precipitated from the solution. The acid was filtered off, washed with water, dried and crystallised from petrol (60/80°)-benzene as prisms (m.p. 217° decomp.). Two further recrystallisations from the same solvent gave, 1,2,4a,9a-tetrahydro-3,4-benzfluorene-9-acetic acid as colourless prisms (m.p. 218-9° decomp., 4g.).

Analysis

$C_{19}H_{18}O_2$ requires C, 81·89; H, 6·52%

found C, 81·60; H, 6·60%

Infrared spectrum (cm^{-1}.)

1715 (s)

(CO_2H)

The Arndt-Eistert Reaction:

A suspension of 1,2,4a,9a-tetrahydro-3,4-benzfluorene-9-acetic acid (XXXVII, m.p. 218°, 1·5g.) in dry ether (20 ml.) containing pyridine (2 drops) was treated at room temperature with redistilled thionyl chloride (1·5 ml.),

and the mixture allowed to stand for 2 hours with occasional shaking. During this time the acid dissolved and the acid chloride precipitated from the solution. The solvent and excess reagent were then removed under reduced pressure on a steam-bath at 40-45° and the last traces of thionyl chloride removed by distillation with benzene (3 x 20 ml.), under the same conditions.

A suspension of the acid chloride in dry ether (60 ml.) was treated with excess diazomethane (1·5g.) in ether (100 ml.) and the reaction mixture allowed to stand at room temperature for 5 hours. Evaporation of the ether under reduced pressure on a water-bath (30°) gave the diazoketone, light-yellow needles (I.R. spectrum -CH-N_2, 2140 cm^{-1}., C=O 1635 cm^{-1}.) which was dissolved in absolute methanol (30 ml.).

This solution was added to a mixture of absolute methanol (20 ml.) and silver oxide (250 mg.) which had been previously boiled until a silver mirror formed. The mixture was boiled under reflux for 30 minutes, another portion of silver oxide (250 mg.) added, and heating continued for a total of 2½ hours. Upon cooling, the reaction mixture was filtered through celite, and the methanol evaporated under reduced pressure to yield a brown gum. Chromatographic purification on a short column of alumina, gave on elution with benzene, a colourless oil which crystallised from petrol (40/60°) as needles (m.p. 96-8°). Two further recrystallisations from the same solvent gave

methyl 1,2,4α9α-tetrahydro-3,4-benzfluorene-9-propionate (LXIII) as colourless needles (m.p. 99-100°, 950 mg.).

Analysis

$C_{21}H_{22}O_2$ requires C, 82·32; H, 7·24%

found C, 82·47; H, 6·80%

Infrared spectrum (cm^{-1}.)

1740 (s)

(satd. ester)

Preparation of 1,2,4α,9α-tetrahydro-3,4-benzfluorene-9-propionic acid (LXIV):

Methyl 1,2,4α,9α-tetrahydro-3,4-benzfluorene-9-propionate (m.p. 98-9°, 500 mg.) in methanol (30 ml.) was boiled under reflux with sodium hydroxide (6g.) in water (15 ml.) for 2 hours. The methanol was removed by distillation, the sodium salt of the acid dissolved in water and extracted with ether. The aqueous alkaline layer was separated, and acidified with hydrochloric acid which precipitated a white solid. This material was filtered off, washed with water, dried, and crystallised from glacial acetic acid as colourless needles (m.p. 203-5° decomp.). One further recrystallisation from the same solvent gave 1,2,4α,9α-tetrahydro-3,4-benzfluorene-9-propionic acid as rosettes (m.p. 206-8° decomp., 350 mg.).

Analysis

$C_{20}H_{20}O_2$ requires C, 82·15; H, 6·89%

found C, 82·30; H, 6·67%

Infrared spectrum (cm^{-1}.)

1715 (s)

(satd. acid)

Preparation of 1,2,3,4,9,12,13,14-Octahydro-10,11-benzfluoranthene-4-one (LXV):

(1) Attempted ring closure with hydrogen fluoride:

1,2,4a,9a-Tetrahydro-3,4-benzfluorene-9-propionic acid (LXIV, m.p. 203-5°, 250 mg.) was suspended in hydrogen fluoride (15 ml.) contained in a polythene vessel. After 18 hours at 10° the cover was removed to allow the hydrogen fluoride to evaporate off, and any remaining traces of hydrogen fluoride were neutralised with ammonium hydroxide solution. The solid material remaining was extracted into benzene-ether (1:1, 200 ml.). Extraction of this solution with saturated sodium bicarbonate solution, gave on acidification a quantity of unchanged acid (m.p. 200-2°, decomp., 200 mg.). Evaporation of the neutral organic phase gave a trace of yellow oil which did not crystallise.

(2) Ring closure by means of the inverse Friedel-Crafts method:

The acid (m.p. 203-5°, 3·8g.) was suspended in dry ether (75 ml.) containing pyridine (1 drop), and treated with redistilled thionyl chloride (6 ml.). The reaction mixture was allowed to stand at room temperature for 2 hours with occasional shaking. The ether and excess thionyl chloride were removed under reduced pressure on a water-bath (30-40°), and all traces of thionyl chloride were removed by distillation under the same condition with benzene (3 x 20 ml.).

A solution of the acid chloride in sym-tetrachloroethane (40 ml.) was added dropwise (10 minutes) to anhydrous stannic chloride (18 ml.) in sym-tetrachloroethane (20 ml.), and the mixture heated at 90° for 45 minutes, then allowed to cool slowly to room temperature (2 hours). The complex was decomposed with cold dilute hydrochloric acid, and extracted with ether-benzene (1:1, 300 ml.). The ethereal extract was washed with hydrochloric acid (20%, 2 x 100 ml.), potassium hydroxide (5%), water, dried and evaporated to dryness to yield a brown gum. Chromatographic purification on a short column of alumina, gave, on elution with benzene, an almost colourless solid which crystallised from petrol (60/80°)-benzene as prisms (m.p. 223-5°). Recrystallisation

from the same solvent gave 1,2,3,4,9,12,13,14-octahydro-10, 11-benzfluoranthene-4-one (LXV), as colourless prisms (m.p. 227-9°, 2·8g.).

Analysis

$C_{20}H_{18}O$ requires C, 87·56; H, 6·61%
found C, 87·32; H, 6·51%

Infrared spectrum (cm^{-1}.)

1680 (s)
(6-ring C=O)

Preparation of 1,2,3,4,9,12,13,14-Octahydro-10,11-benzfluoranthen-4-hydrazone (LXVI):

The ketone (LXV, m.p. 223-5°, 600 mg.) was suspended in absolute ethanol (40 ml.) and boiled under reflux for 15 minutes, during which the ketone gradually passed into solution. Hydrazine hydrate (99%, 2 ml.) was added, and the mixture refluxed for 1 hour. Ethanol (20 ml.) was then distilled off, and the solution allowed to cool. The hydrazone crystallised out of the solution as colourless prisms (m.p. 206-8°, 580 mg.).

Analysis

$C_{20}H_{20}N_2$ requires N, 9·71%
found N, 9·51%

Infrared spectrum (cm^{-1}.)

3400 (w) 1610 (w)
(NH_2) (C=N)

Preparation of 1,2,3,4,9,12,13,14-Octahydro-10,11-benzfluoranthene A.

The hydrazone (LXVI, m.p. 202-3°, 500 mg.) was added to a solution of potassium hydroxide (2g.) in ethylene glycol (50 ml.) and the mixture boiled under reflux for 3 hours. After this time 10 ml., of distillate was removed using a Dean and Stark separator. Upon cooling fine white needles precipitated from the distillate (m.p. 145-7°). It thus appeared that the hydrocarbon product was volatile in the ethylene glycol. This facile separation was exploited and more ethylene glycol (50 ml.) introduced into the reaction flask and subsequently distilled off. The ethylene glycol distillate (90 ml.) was diluted with water (300 ml.) and the white precipitate extracted into ether. The ether solution was washed with water, dried and evaporated to dryness to yield a white solid. This was recrystallised from ethanol as needles (m.p. 144-6°) and one further recrystallisation from the same solvent gave 1,2,3,4,9,12,13,14-octahydro-10,11-benzfluoranthene A, as colourless needles (m.p. 149-50°, 320 mg.).

Analysis

$C_{20}H_{20}$	requires	C, 92·26;	H, 7·74%
	found	C, 92·07;	H, 7·56%

The N.M.R. Spectrum shows a ratio of 7 aromatic:13 other protons.

Preparation of 10,11-Benzfluoranthene (II).

1,2,3,4,9,12,13,14-Octahydro-10,11-benzfluoranthene A (m.p. 149-50°, 250 mg.) was dissolved in benzene (50 ml.) containing tetrachloro-o-quinone (1g.) and the mixture boiled under reflux for 2 hours, during which time the deep-red colour of the o-quinone disappeared to give a light-yellow solution. The solution was cooled and filtered through a short column of alumina (20 g.). A yellow band was eluted in benzene and on evaporation gave a yellow oil which solidified on trituration with petrol (60/80°). Recrystallisation from petrol (60/80°)-benzene gave 10,11-benzfluoranthene (II) as yellow needles (m.p. 163-5°, 200 mg.). The picrate (red-brown needles) melted at 195°. Both the hydrocarbon and the corresponding picrate showed no depression on admixture with authentic material.

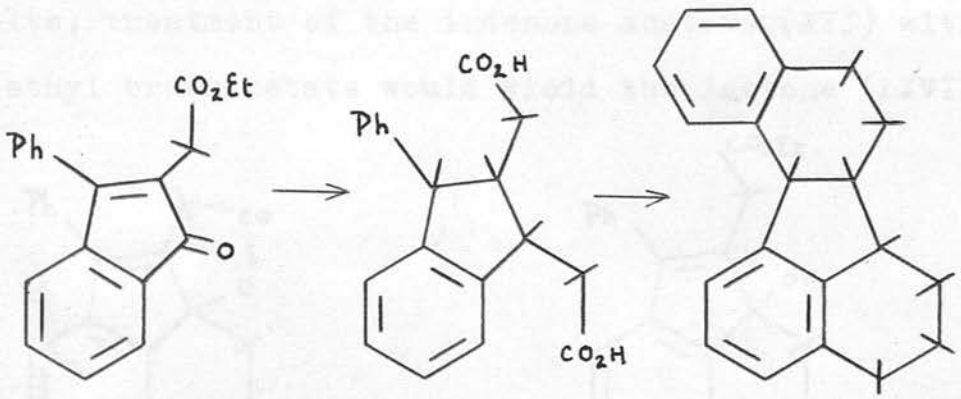
PART II

Intermediates derived from Ethyl 3-phenylindene-1-one-2-acetate (XXI).

(1) The Reformatsky reaction.

(2) Condensation with Malononitrile.

This section describes the earlier unsuccessful work towards a synthesis of the octahydro-10,11-benzfluoranthene A. It involved direct addition to the indenone nucleus (XXI), and the synthetic ideas behind this approach are represented schematically below:-

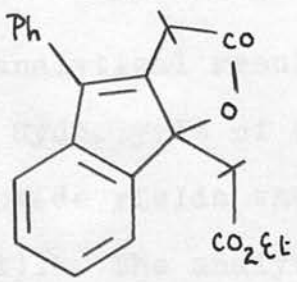


XXI LXVII A

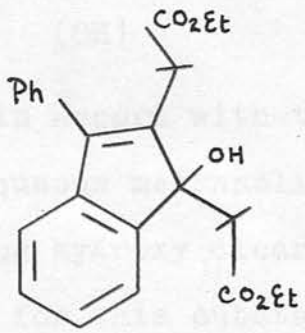
Introduction of a side chain at the 1-position (by standard methods considered in Part I) followed by hydrogenation and hydrolysis, would give 3-phenylindan-1,2-diacetic acid (LXVII). This could then be converted into the octahydro-10,11-benzfluoranthene A. The intermediates isolated during this work will now be described.

(1) The Reformatsky reaction on Ethyl 3-phenylindene-1-one-2-acetate (XXI):

Dreiding and Tomasewski (31) and Bachmann (32, 33) have reported that γ-keto esters undergo the Reformatsky reaction with zinc and methyl bromoacetate to yield lactone esters, and not the normal β-hydroxy ester. On the basis of their results, treatment of the indenone acetate (XXI) with zinc and ethyl bromoacetate would yield the lactone (LXVIII).

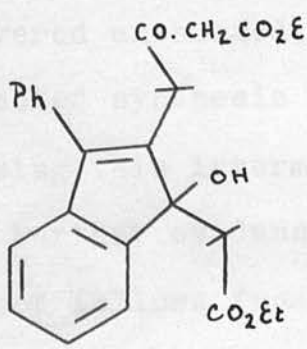


LXVIII

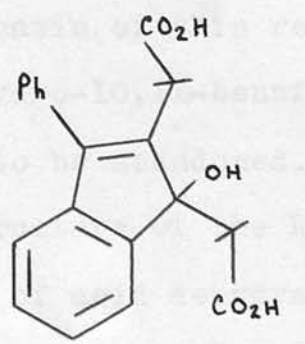


LXIX

The product of the reaction, however, shows properties consistent with structure (LXIX), i.e., the normal β-hydroxy ester. It is a colourless solid (m.p. 79-80°), and is isolated in about 60% yield. Kidd (34) suggested that the product from the above reaction was (LXX) resulting from



LXX



LXXI

attack on the carbonyl group of the ester (37), to account for his ambiguous analytical results. This structure can now be discounted from the evidence of the infrared spectrum of the product (LXIX), which shows absorption bands at 3450, 1735, and 1675 cm^{-1}. which correspond to the hydroxyl, saturated ester and C=C groupings respectively. The N.M.R. spectrum shows the following ratio of protons:-

9	:	8	:	1	:	6
(aromatic)		(CH_2)		(OH)		(CH_3)

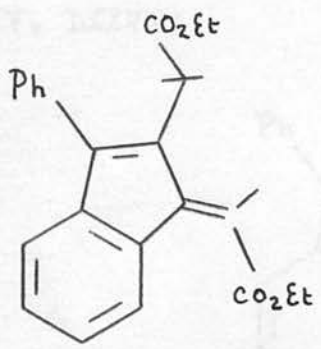
The analytical results are also in accord with this structure.

Hydrolysis of (LXIX) with aqueous methanolic sodium hydroxide yields the corresponding hydroxy dicarboxylic acid (LXXI). The analytical results for this substance would suggest that the hydroxy ester is sensitive to alkali, and possibly undergoes partial cleavage during hydrolysis (35) with the formation of 3-phenylindene-1-one-2-acetic acid, although this acid was not in fact isolated.

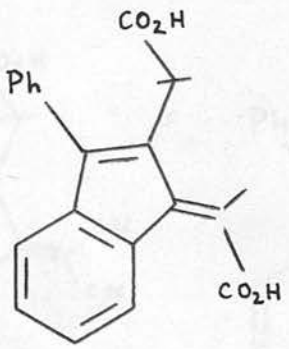
The Reformatsky product (LXIX) was subjected to catalytic hydrogenation using Adams and Raney nickel catalysts. In both experiments the hydroxy ester was recovered unchanged, and on the basis of this result, the projected synthesis of the octahydro-10,11-benzfluoranthene A, using this intermediate, had to be abandoned.

Further evidence for the structure of the Reformatsky product follows from the results of acid dehydration. This

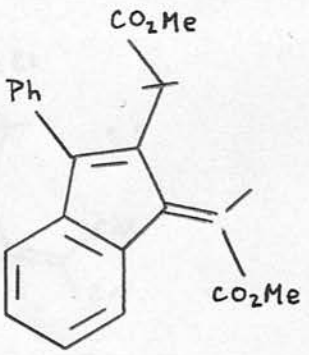
would produce the highly coloured benzofulvene system, and this is indeed observed. When the hydroxy ester (LXIX) is heated with 90% formic acid, a low melting orange solid (LXXII) was isolated in high yield.



LXXII



LXXIII

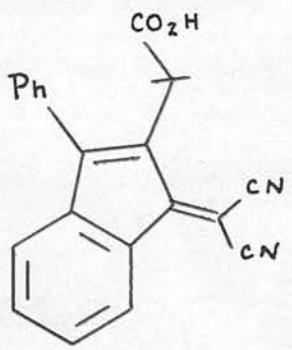


LXXIV

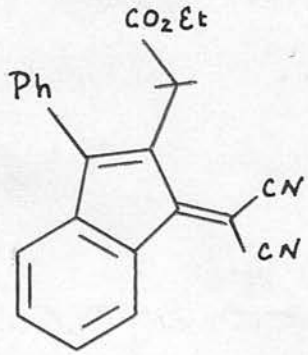
The infrared spectrum of this substance shows bands corresponding to the saturated, α,β-unsaturated ester groupings, and phenyl conjugated diene system at 1740, 1720, and 1625 cm^{-1}. respectively. Hydrolysis of (LXXII) with aqueous methanolic sodium hydroxide gave the corresponding deep-red dicarboxylic acid (LXXIII), which on esterification with concentrated sulphuric acid - absolute methanol, produced the orange dimethyl ester (LXXIV).

(2) Condensation with Malononitrile:

3-Phenylindene-1-one-2-acetic acid and its ethyl ester (XXI) readily condense with malononitrile in benzene solution containing a base (36), e.g., pyridine, piperidine etc., yielding the corresponding dicyanomethylene derivatives (LXXV, LXXVI).

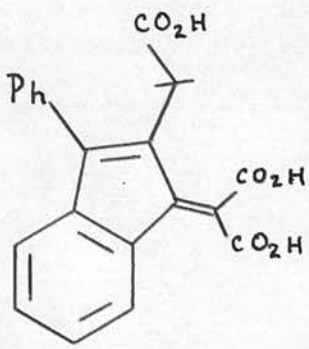


LXXV

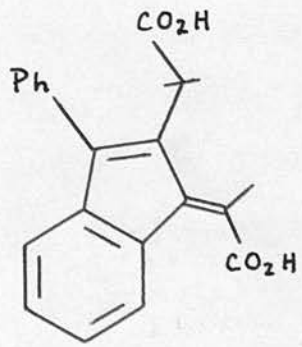


LXXVI

These are dark-red solids, and their infrared spectra show peaks at 2235 (CN), 1740, 1720 (C=O, ester and acid), 1600, 1570 cm^{-1}. (C=C). The analytical results are in accord with the above structures.



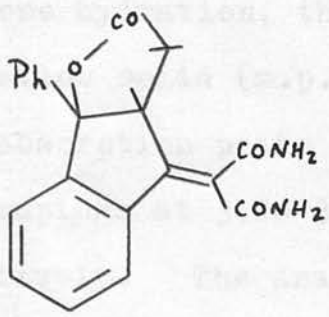
LXXVII



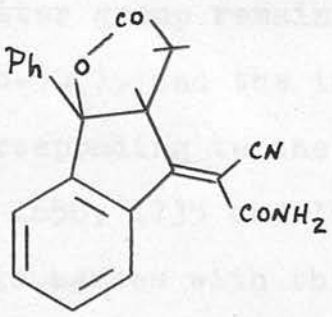
LXXIII

The hydrolysis of these dicyano compounds is complicated. This type of hydrolysis apparently does not produce the tricarboxylic acid (LXXVII), which would decarboxylate to give the dicarboxylic acid (LXXIII), and this alternative synthetic route to the dibasic acid was therefore abandoned. A variety of hydrolysing conditions were considered, and tentative structures assigned to the products isolated from the hydrolysis of the dicyano ester (LXXVI).

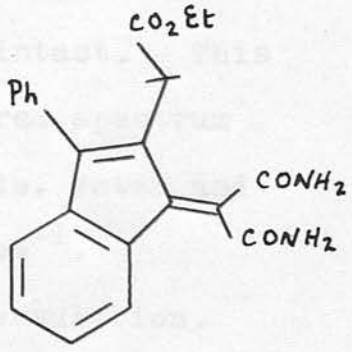
Hydrolysis of the Dicyano ester (LXXVI):



LXXVIII



LXXIX



LXXX

(i) Heating with 70% sulphuric acid yields a mixture of unchanged material and a white solid (m.p. 196-8°). Loss of colour indicates lactone formation during hydrolysis. The infrared spectrum shows absorption at 3400, 3200 (NH_2), 1750 (C=O, γ-lactone), 1650 (C=O, amide) and 1580 cm^{-1}. (C=C). The analysis is in agreement with structure (LXXVIII).

(ii) Heating with 70 sulphuric acid using twice the

weight of the dinitrile. Under these conditions the lactone (LXXIX), white needles (m.p. 238-40°) is produced. The analytical results agree with this structure, and the infrared spectrum shows absorption at 3475, 3350 (NH_2), 2220 (CN), 1770 (C=O, γ-lactone), 1670 (C=O, amide), and 1575 cm^{-1}. (C=C). This compound is stable to concentrated sulphuric acid at room temperature.

(iii) With concentrated sulphuric acid at room temperature, (LXXX) is isolated as the product, both cyano groups have undergone hydration, the ester group remaining intact. This is a yellow solid (m.p. 248-50°), and the infrared spectrum shows absorption peaks corresponding to the amide, ester and C=C groupings at 3400 3200 1650, 1735 and 1625 cm^{-1}. respectively. The analysis agrees with this formulation.

(iv) Heating with sulphuric acid-acetic acid-water (10:7:2) for four hours at 100° produces a mixture of (LXXIX) and (LXXX) together with a small amount of a red solid (m.p. above 300°) of unknown composition.

Further hydrolysis with 20% methanolic potassium hydroxide, or 10% potassium hydroxide in ethylene glycol produced red gums which did not crystallise from the usual solvents.

On the basis of the above results, this synthetic approach was discarded in favour of addition to the indane nucleus described in Part I.

EXPERIMENTAL PART II

The Reformatsky reaction on Ethyl 3-phenylindene-1-one-2-acetate (XXI):

Ethyl 3-phenylindene-1-one-2-acetate (m.p. 80-2°, 10g.) was dissolved in benzene-ether (1:1, 100 ml.) and zinc wool (10g.), ethyl bromoacetate (13·5 ml.) added to the solution. A crystal of iodine was added and the reaction initiated by gentle warming on a water-bath. After refluxing for 30 minutes, further amounts of zinc wool (10g.), ethyl bromoacetate (6·5 ml.) were added, and reflux maintained for a further three hours. On cooling, the reaction mixture was treated with ice and acetic acid, the organic material separated off, and the residual zinc washed by decantation with benzene-ether (1:1, 3 x 50 ml.). The combined extracts were then washed successively with water, dilute ammonium hydroxide (until the washings were colourless), finally washed with water, dried and evaporated to dryness to yield a red-brown gum (12g.). Chromatographic purification on alumina (50g.) produced an almost colourless oil (8g.) on evaporation of the benzene eluates. This material crystallised from petrol (60/80°)-benzene as colourless prisms (m.p. 76-8°). One further recrystallisation from petrol (60/80°) gave ethyl 3-phenylindene-1-ol-1,2-diacetate (LXIX) as prisms (m.p. 78-80°, 6·5g.).

Analysis

$C_{23}H_{24}O_5$	requires	C, 72·6;	H, 6·30%
	found	C, 72·0;	H, 6·23%

Infrared spectrum (cm^{-1}.)

3450 (m)	1735 (s)	1675 (w)
(OH)	(C=O satd. ester)	(C=C)

Preparation of 3-Phenylindene-1-ol-1,2-diacetic acid (LXXI):

The hydroxy ester (LXIX, m.p. 79-80°, 1g.) was dissolved in methanol (20 ml.) and boiled under reflux with potassium hydroxide (3g.) in water (10 ml.) for 2 hours. Methanol (15 ml.) was distilled off with simultaneous addition of water (15 ml.). The solution was diluted with water (100 ml.), extracted with ether, and the neutral ethereal extract removed. The aqueous alkaline phase was acidified with hydrochloric acid, and a yellow solid precipitated from the solution. This material was filtered off, washed with water, dried and crystallised from benzene as needles (m.p. 173-5° decomp.). Two recrystallisations from the same solvent gave 3-phenylindene-1-ol-1,2-diacetic acid (LXXI) as light-yellow needles (m.p. 178-9°, 700 mg.).

Analysis

$C_{19}H_{16}O_5$	requires	C, 70·5;	H, 4·95%
	found	C, 72·2;	H, 5·28%

Infrared spectrum (cm^{-1}.)

3600 (m)	1710 (s)	1650 (w)
(OH)	(C=O satd. acid)	(C=C)

Catalytic reduction of Reformatsky Product:

(a) Adams Catalyst:

The hydroxy ester (LXIX, m.p. 79-80°, 1g.) in ethanol (50 ml.) was introduced into a hydrogenation flask containing Adams catalyst (100 mg.) suspended in ethanol (50 ml.) and the mixture shaken under hydrogen at one atmosphere pressure for 1½ hours. The catalyst was filtered off, and the ethanol evaporated under reduced pressure to yield a colourless oil. This was dissolved in petrol (60/80°) and crystallised to give ethyl 3-phenylindene-1-ol-1,2-diacetate (LXIX) as colourless prisms (m.p. and mixed m.p. 78-80°, 900 mg.).

(b) Raney Nickel:

Hydrogenation was carried out under exactly similar conditions, using Raney nickel as the catalyst. Once again the hydroxy ester (LXIX) was recovered in good yield.

Dehydration of the Reformatsky Product:

The hydroxy ester (LXIX, m.p. 79-80°, 2g.) was dissolved in 90% formic acid (30 ml.) and heated at 100° for 2 hours

giving an orange solution. The reaction mixture was poured into water (150 ml.) and extracted with ether. The ethereal solution was washed with water, 10% sodium bicarbonate solution, water, dried and evaporated to dryness to give an orange gum. Chromatographic purification on alumina (10g.) gave an orange oil (1·7g.) on evaporation of the petrol (60/80°)-benzene (1:2) eluates. This material crystallised from petrol (40/60°) as matted orange prisms (m.p. 65-8°). One recrystallisation from the same solvent gave the unsaturated di-ester (LXXII) as orange prisms (m.p. 67-9°, 1·55g.).

Analysis

$C_{23}H_{22}O_4$	requires	C, 76·03;	H, 6·06%
	found,	C, 76·18;	H, 5·70%

Infrared spectrum (cm^{-1}.)

1740 (s)	1720 (s)	1625 (m)
(C=O, satd. ester)	(C=O α,β-unsatd. ester)	(C=C)

Hydrolysis of the Unsaturated Di-ester (LXXII):

A solution of the diethyl ester (LXXII, m.p. 66-8°, 1·2g.) in methanol (15 ml.) was boiled under reflux with potassium hydroxide (2g.) in water (4 ml.) for 2 hours. Methanol (10 ml.) was distilled off with simultaneous addition of water (10 ml.). The solution was diluted with water (100 ml.), extracted with ether, and the neutral

ethereal extract removed. The aqueous alkaline phase was acidified with hydrochloric acid, and a red solid precipitated from the solution. This material was filtered off, washed with water, dried, and crystallised from acetone containing a trace of benzene to give the unsaturated dicarboxylic acid (LXXIII) as dark-red micro prisms (m.p. 278-80° decomp. 900 mg.).

Analysis

$C_{19}H_{14}O_4$	requires	C, 74·5; H, 4·57%
	found	C, 73·7; H, 4·80%

Infrared spectrum (cm^{-1}.)

1710 (s)	1680 (s)	1625 (m)
(C=O, satd. acid)	(C=O, α,β-unsatd. acid)	(C=C)

Preparation of the Dimethyl Ester (LXXIV):

A suspension of the unsaturated acid (LXXIII, m.p. 278-80°, 500 mg.) in absolute methanol (50 ml.) was treated dropwise with concentrated sulphuric acid (2 ml.) and the mixture refluxed for 2 hours. Methanol (30 ml.) was distilled off, with simultaneous addition of water (30 ml.), and the reaction mixture poured into water (150 ml.), and extracted with ether. The ethereal solution was washed with dilute sodium hydroxide solution, water, dried and evaporated to dryness to give a red oil (400 mg.). Chromatographic purification on alumina (5g.) gave an orange oil on

evaporation of the petrol (60/80°)-benzene (1:2) eluates. This material crystallised from petrol (40/60°) to give the unsaturated dimethyl ester (LXXIV) as orange prisms (m.p. 98-100°, 300 mg.).

Analysis

$C_{21}H_{18}O_4$	requires	C, 75·5; H, 5·40%
	found	C, 75·5; H, 5·46%

Infrared spectrum (cm^{-1}.)

1730 (s)	1710 (s)	1635 (m)
(C=O, satd. ester)	(C=O, α,β-unsatd. ester)	(C=C)

Condensation with Malononitrile:

A solution of 3-phenylindene-1-one-2-acetic acid (m.p. 162-4°, 3g.) in benzene (25 ml.), pyridine (15 ml.), was treated with malononitrile (2.5g.) and the mixture boiled under reflux for 1 hour. The cold dark-red solution was diluted with water (150 ml.) and extracted with ether, and the ethereal solution washed with hydrochloric acid (5%), water, then acidic material extracted with sodium hydroxide solution (5%). Acidification of the alkaline extract with hydrochloric acid precipitated an oily red solid. This was dissolved in ether and the ethereal solution washed with water, dried and evaporated to dryness to give a dark-red gum. This material crystallised from petrol

(60/80°)-benzene as red needles (m.p. 170-3°). Two further recrystallisations from the same solvent gave 3-phenylindene-1-dicyanomethylene-2-acetic acid (LXXV) as dark-red needles (m.p. 186-8°, 3g.).

Analysis

$C_{20}H_{12}N_2O_2$	requires	C, 76·9;	H, 3·85;	N, 8·97%
	found	C, 76·6;	H, 4·50;	N, 7·30%

Infrared spectrum (cm^{-1}.)

2235 (m)	1720 (s)	1600, 1570 (m)
(CN)	(C=O, satd. acid)	(C=C).

Preparation of Ethyl 3-phenylindene-1-dicyanomethylene-2-acetate (LXXVI):

A solution of ethyl 3-phenylindene-1-one-2-acetate (XXI, m.p. 80-2°, 1g.) in benzene (25 ml.), pyridine (15 ml.) was treated with malononitrile (1g.), and the mixture boiled under reflux for 1 hour. The water produced during the reaction was removed by adding and distilling off benzene (25 ml.). The cold dark-red solution was diluted with water (150 ml.), and extracted with ether. The ethereal solution was washed with hydrochloric acid (5%), water, dried and evaporated to yield a dark-red oil which crystallised from petrol (60/80°) as dark-red needles (m.p. 108-10°). One further recrystallisation from the

same solvent gave ethyl 3-phenylindene-1-dicyanomethylene-2-acetate (LXXVI) as dark-red needles (m.p. 111-13°, lg.).

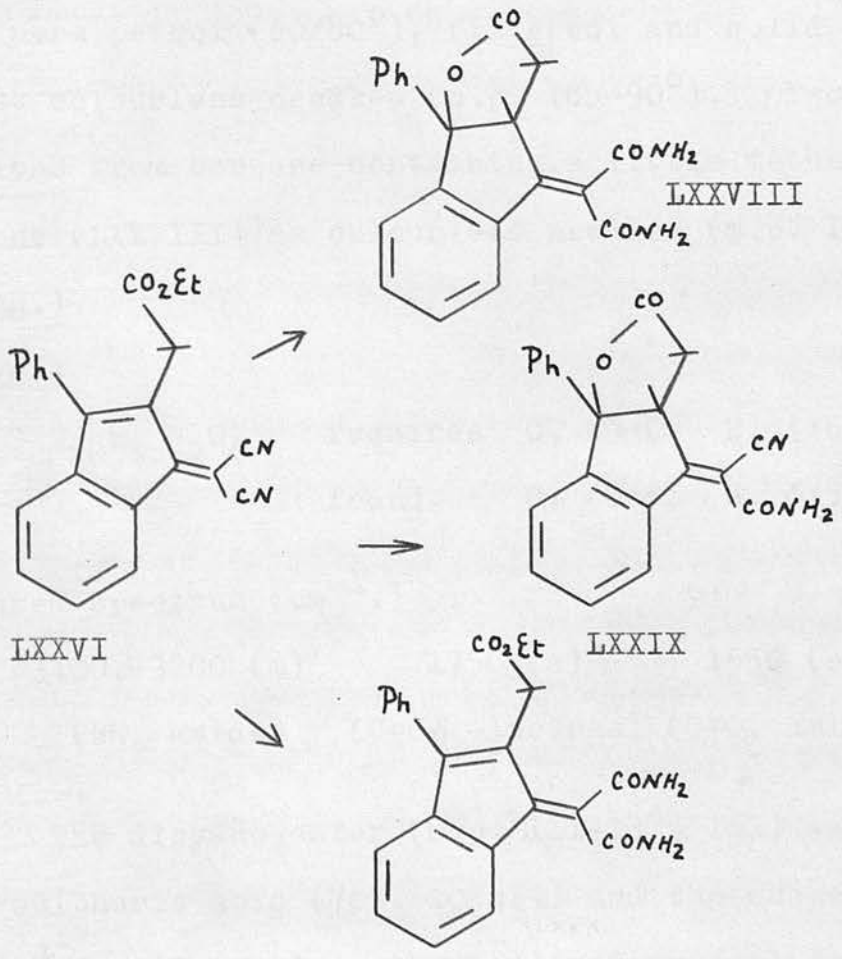
Analysis

$C_{22}H_{16}N_2O_2$	requires	C, 77·64;	H, 4·70;	N, 8·24%
	found	C, 77·76;	H, 4·88;	N, 7·90%

Infrared spectrum (cm^{-1}.)

2235 (m)	1740 (s)	1600, 1570 (m)
(CN)	(C=O satd. ester)	(C=C)

Hydrolysis of Dicyano-Ester (LXXVI):



(i) 70% Sulphuric Acid:

(a) The dicyano-ester (m.p. 111-13°, 1g.) was dissolved in warm sulphuric acid (70%, 20 ml.) and the mixture heated at 100° for 15 minutes, then allowed to cool to room temperature. The unchanged dicyano-ester (m.p. and mixed m.p. 110-12°, 600 mg.) was filtered off, and the filtrate diluted with water (150 ml.). The pink precipitate was extracted with benzene, and the benzene solution washed with sodium hydroxide (5%), water, dried and evaporated to dryness to give a residual pink solid. This was triturated with warm petrol (60/80°), filtered, and solid dried to give almost colourless needles (m.p. 185-90°). Two recrystallisations from benzene containing a little methanol gave the lactone (LXXVIII) as colourless needles (m.p. 198-200°, 150 mg.).

Analysis

$C_{20}H_{16}N_2O_4$	requires	C, 69·0;	H, 4·60;	N, 8·03%
	found	C, 68·5;	H, 4·53;	N, 7·60%

Infrared spectrum (cm^{-1}.)

3400, 3200 (m)	1750 (s)	1650 (s)	1580 (m)
(NH_2 amide)	(C=O δ -lactone)	(C=O, amide)	(C=C)

(b) The dicyano-ester (m.p. 111-13°, 1g.) was suspended in warm sulphuric acid (70%, 10 ml.) and the suspension heated at 100° for 15 minutes, then allowed to cool to room

temperature. The unchanged dicyano-ester (m.p. and mixed m.p. 110-12°, 750 mg.) was filtered off, and the greenish-red solution diluted with water (150 ml.). The pink precipitate was washed with water, dried and washed with hot petrol (60/80°), and crystallised from dioxan-petrol (60/80°) as colourless needles (m.p. 228-32°). Three further recrystallisations from the same solvent gave the lactone (LXXIX) as colourless needles (m.p. 238-40°, 75mg.).

Analysis

$C_{20}H_{14}N_2O_3$	requires	C, 72·7;	H, 4·25;	N, 8·5%
	found	C, 72·2;	H, 4·32;	N, 7·9%

Infrared spectrum (cm^{-1}.)

3475, 3350 (m)	2220 (m)	1770 (s)	1670 (s)	1575 (m)
(NH_2 amide)	(CN)	(C=O, γ-lactone)	(C=O amide)	(C=C)

(ii) Concentrated Sulphuric Acid:

The dicyano-ester (LXXVI, m.p. 111-13°, 1g.) was dissolved in concentrated sulphuric acid (45 ml.) and the mixture allowed to stand at room temperature for 2 hours. The reaction mixture was then poured into water (250 ml.), and the yellow precipitate washed with water, dried, washed with hot petrol (60/80°), and crystallised from dioxan-petrol (60/80°) as yellow plates (m.p. 238-43°). Three recrystallisations from the same solvent gave the lactone

(LXXX) as yellow plates (m.p. 250-2°, 600 mg.).

Analysis

$C_{22}H_{20}N_2O_4$	requires	C, 70·0;	H, 5·30;	N, 7·45%
	found	C, 69·8;	H, 5·20;	N, 6·82%

Infrared spectrum (cm^{-1}.)

3400, 3200 (s)	1735 (s)	1650 (s)	1625 (m)
(NH_2, amide)	(C=O, satd. ester)	(C=O, amide)	(C=C)

(iii) Sulphuric Acid-Acetic Acid-Water:

The dicyano-ester (LXXVI, m.p. 111-13°, 1g.) was suspended in a mixture of sulphuric acid-acetic acid-water (10:7:2, 57 ml.) and the suspension heated at 100° for four hours. The cold mixture was diluted with water (150 ml.) and the precipitate extracted with chloroform. The chloroform solution was washed with water, sodium hydroxide solution, water, dried and evaporated to dryness to yield a yellow solid. This was extracted with boiling benzene (40 ml.), filtered, and the residual yellow plates recrystallised from dioxan-petrol (60/80°) to give the lactone ester (LXXX), as yellow plates (m.p. and mixed m.p. 248-50°, 300 mg.). The benzene filtrate was reduced in volume, and on cooling precipitated colourless needles, identical to the lactone (LXXIX, m.p. and mixed m.p. 236-8°, 75 mg.). Acidification of the alkaline extract with hydrochloric

acid precipitated a small amount of a dark-red solid. This was filtered off, washed with water, dried (75 mg.). This material has a melting-point above 290°, and does not crystallise from the usual solvents. Its constitution has not been established.

Infrared spectrum (cm^{-1}.)

3400, 3200 (w)	1825 (s)	1720, 1680 (s)	1600 (m)
(NH_2, amide)	(C=O, lactone)	(C=O)	(C=C)

(iv) Potassium Hydroxide:

(a) The dicyano-ester (LXXVI, m.p. 111-13°, 1g.) was dissolved in methanol (30 ml.) and boiled under reflux with potassium hydroxide (10g.) in water (13 ml.) for 2 hours. Methanol (20 ml.) was distilled off, water (200 ml.) added and the solution extracted with ether. The ethereal solution was removed and the aqueous alkaline phase acidified with hydrochloric acid. The red oily precipitate was extracted with ether, and the ethereal solution washed with water, dried and evaporated to yield a red gum (850 mg.). This material failed to crystallise from the usual solvents. Its constitution has not been established.

(b) In this experiment the dicyano-ester (LXXVI) was boiled with 10% potassium hydroxide in ethylene glycol. The product of this reaction, an acidic dark-red gum, is of unknown constitution.

Ultraviolet Spectra.

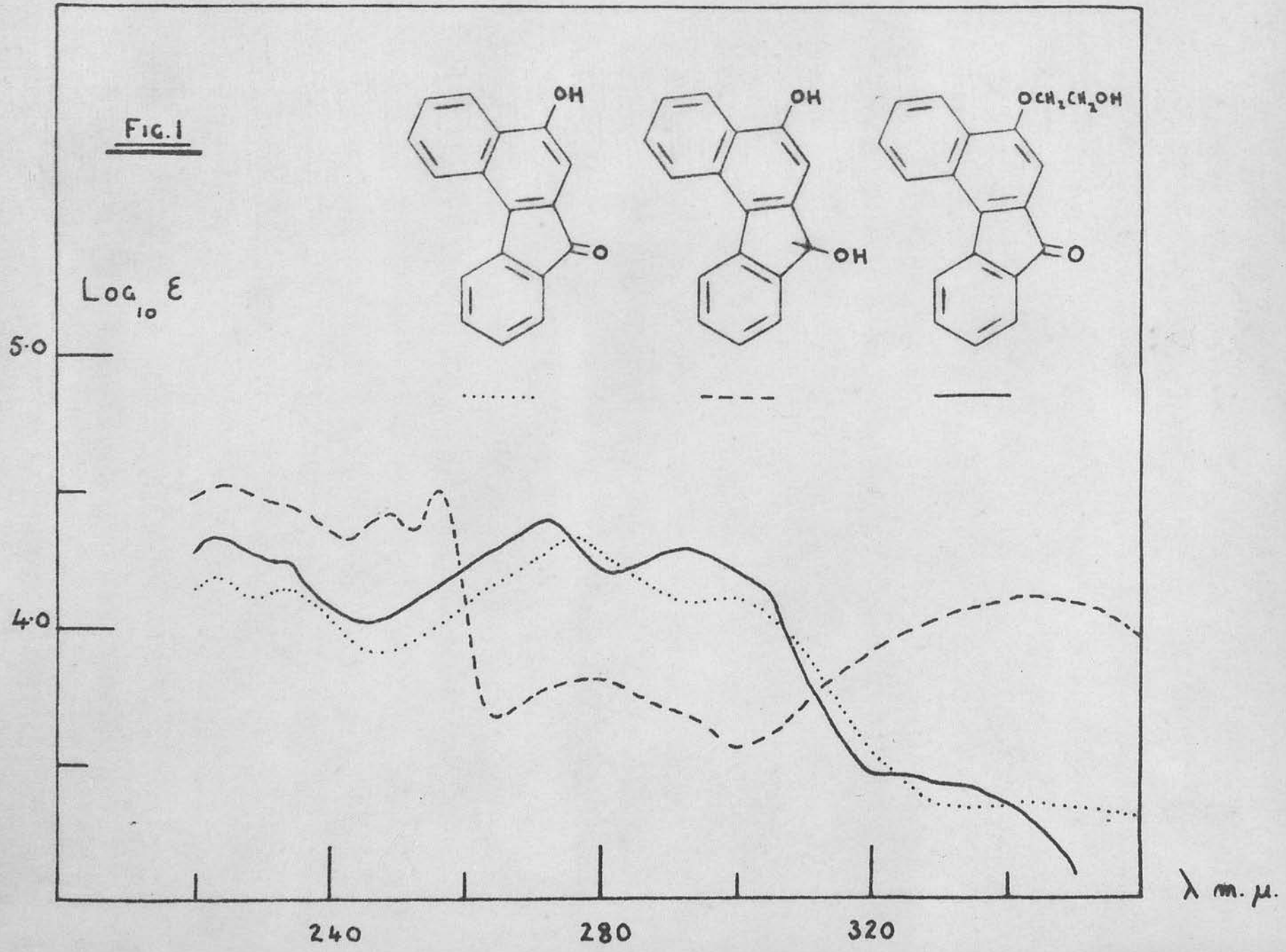


FIG. 1
OH
O
OH
OH
O
OCH2CH2OH
Log10 ε
5·0
4·0
240
280
320
λ m. μ.

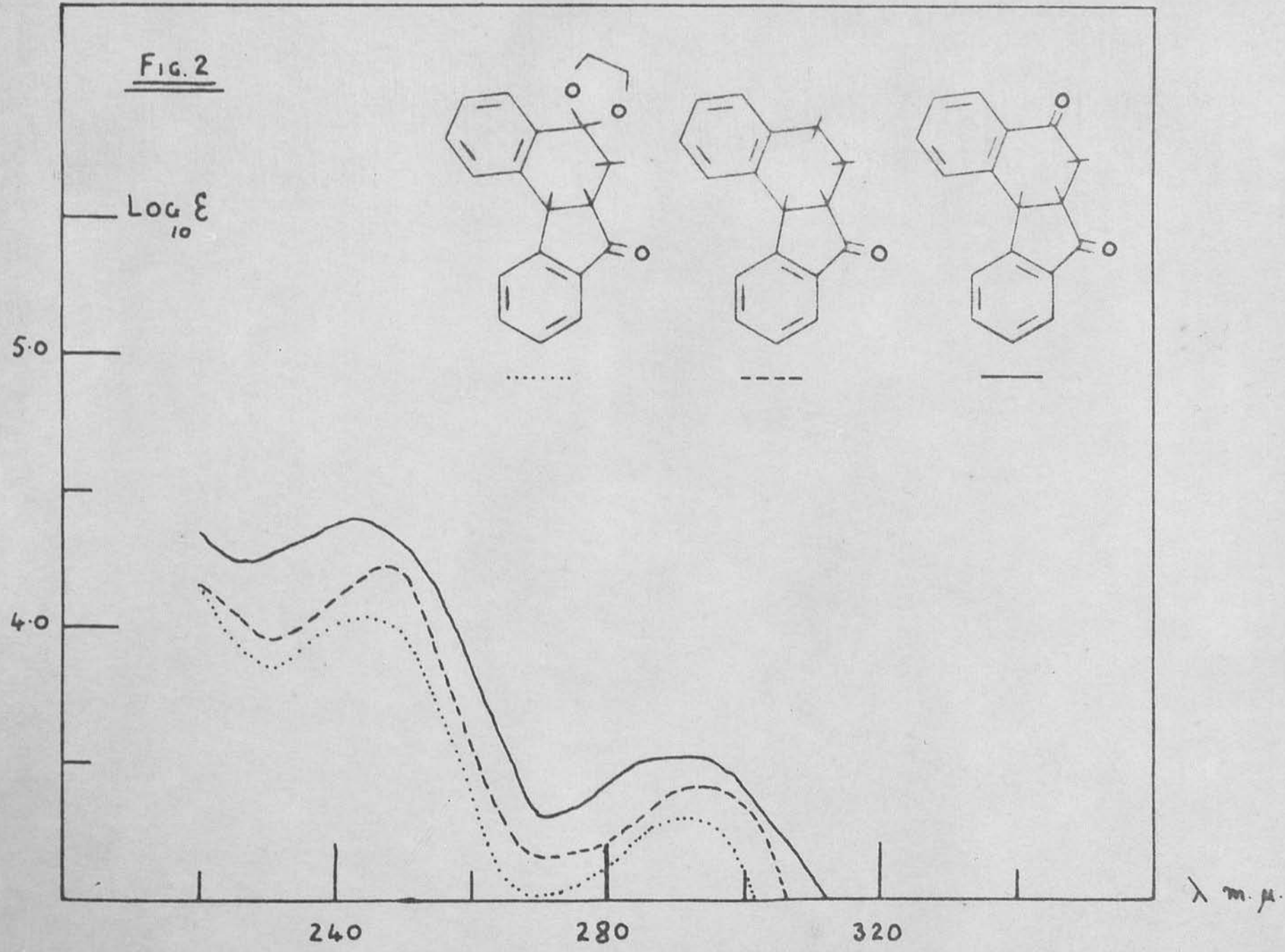


FIG. 2
Log 10 ε
5·0
4·0
240
280
320
λ m. μ.

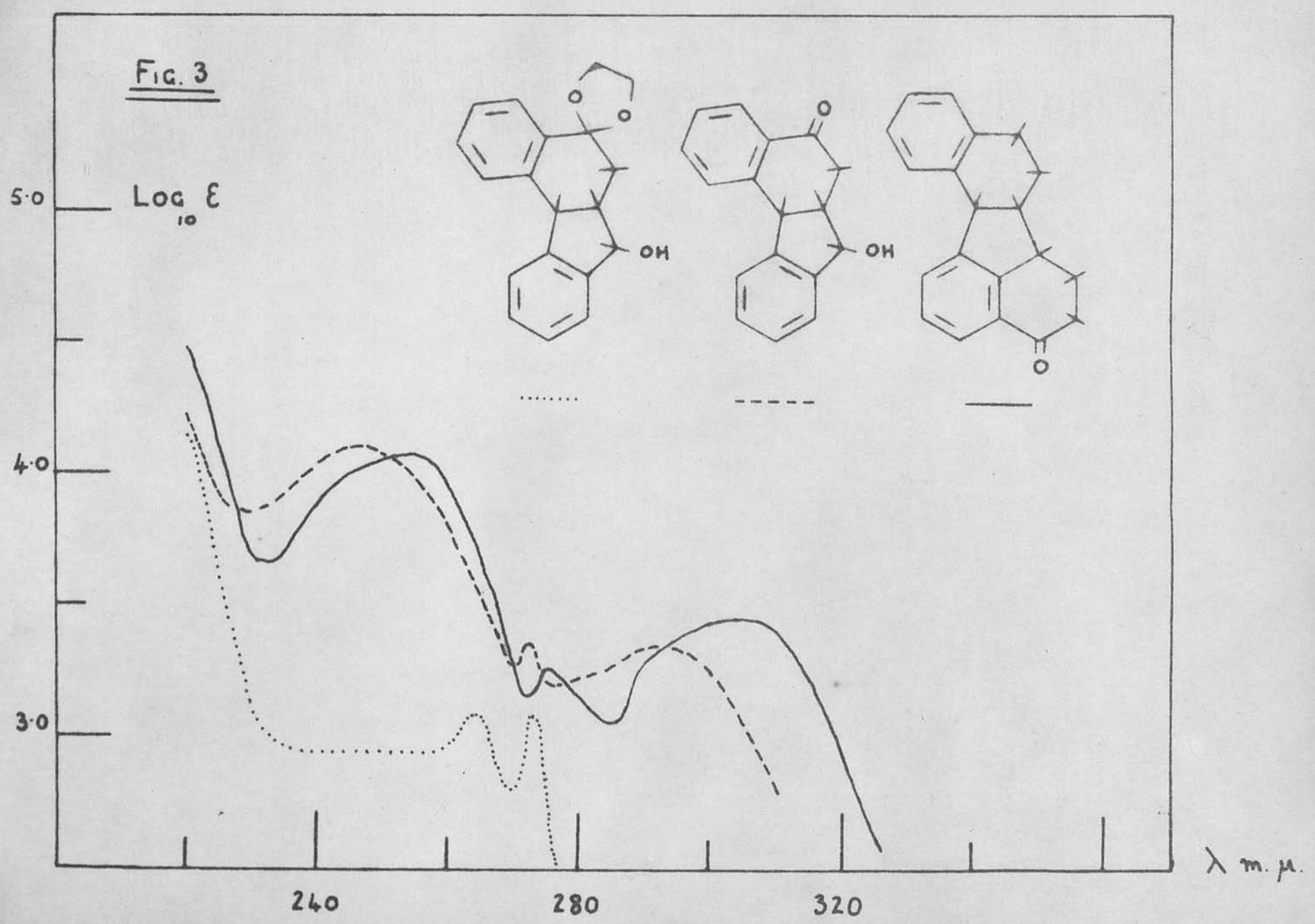


Fig. 3
Log 10 ε
5·0
4·0
3·0
OH
OH
O
O
O
O
240
280
320
λ m. μ.

FIG. 4

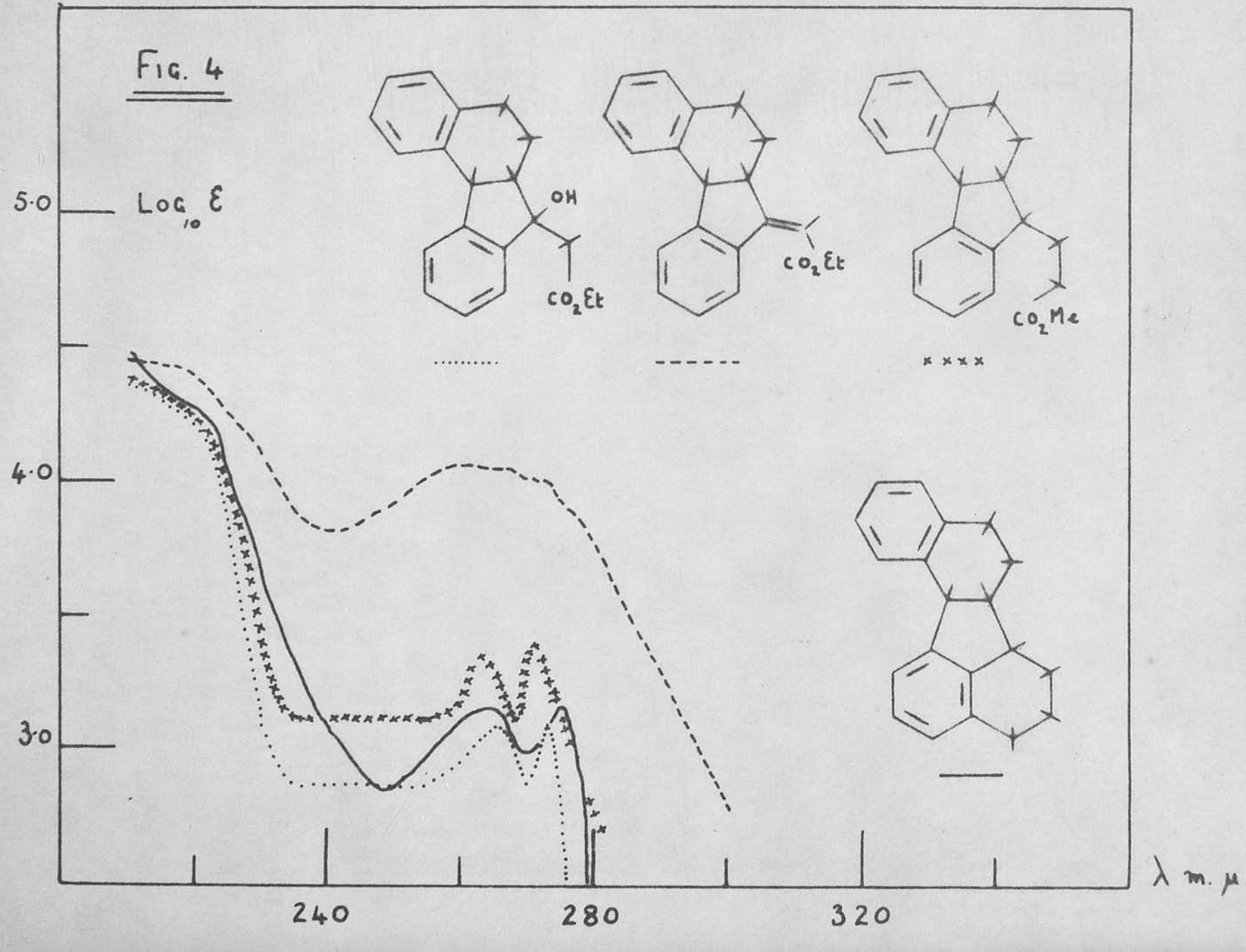
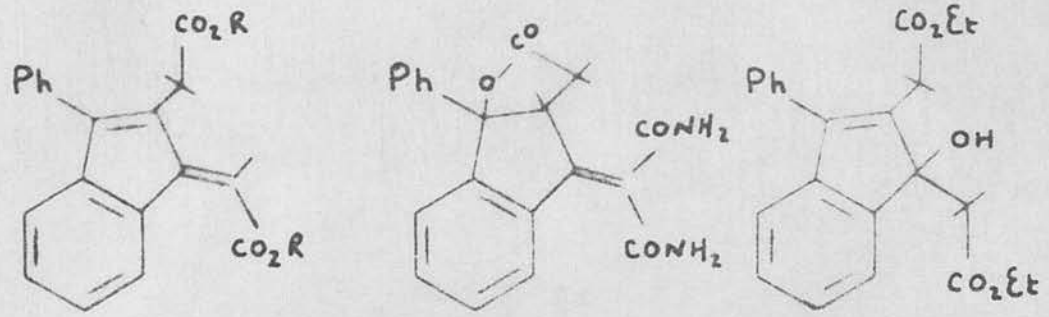


FIG. 5


Ph
CO2R
CO2R
Ph
O
CO
CONH2
CONH2
Ph
CO2Et
OH
CO2Et

R = Me ××××

= Et ····· ----- ——

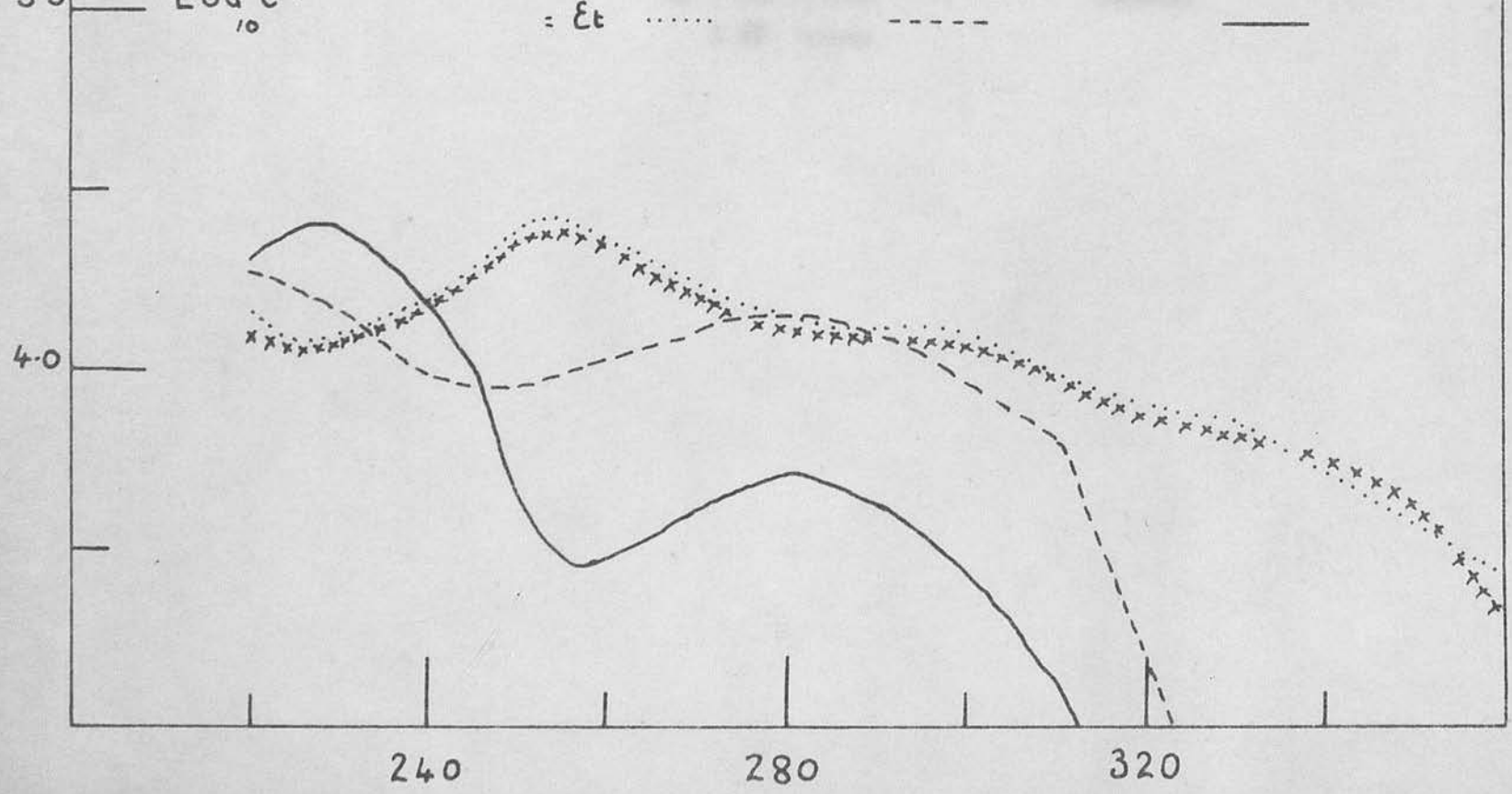
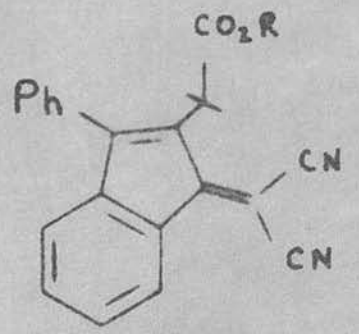
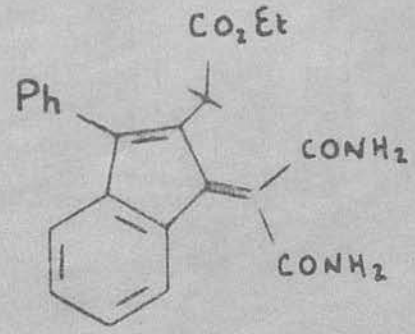

5·0
Log10 ε
4·0
240
280
320
λ m.μ.

Fig. 6





R = Et – – –
= H .....

5·0 Log ε_{10}

4·0

240 280 320 λ m. μ.

BIBLIOGRAPHY

1. von Braun and Kirschbaum, Ber. 1921, 54, 597.
2. Dansi and Ferri, Gazz. chim. ital. 1941, 71, 648.
3. Nenitzescu and Avram, J.A.C.S., 1950, 72, 3486.
4. Bell and Hunter, J.C.S., 1950, 2904.
5. Orchin and Reggel, J.A.C.S., 1947, 69, 505.
6. Moureau, Bull. Soc. Chim. 1948, 99.
7. Orchin and Reggel, J.A.C.S., 1951, 73, 436.
8. Campbell, Kanna and Marks, J.C.S., 1951, 2511.
9. Zinke and Pack, Monatsh, 1949, 80, 213.
10. Woodward and Eastman, J.A.C.S., 1944, 66, 674.
11. Evans and Smith, J.C.S., 1954, 798.
12. Koelsch, J. Org. Chem. 1961, 26, 2590.
13. Loewenthal, Tetrahedron, 6, 269.
14. Poos, Arth, Beyler and Sarett, J.A.C.S., 1953, 75, 422.
15. Salmi, Ber. 1938, 71, 1803.
16. Ringold, J.A.C.S., 1954, 76, 1362.
17. Wadsworth and Emmons, J.A.C.S., 1961, 83, 1733.
18. Lenhard and Bernstein, J.A.C.S., 1956, 78, 989.
19. Rao and Kurath, J.A.C.S., 1956, 78, 5660.
20. Haworth and Woodcock, J.C.S., 1940, 1324.
21. Kidd, Ph.D. thesis Edinburgh University, 1954, p.47.
22. Jones, J.C.S., 1946, 39.

23. Bachmann and Shehnan, J.A.C.S., 1940, 62, 2687.

24. Johnson and Glen, J.A.C.S., 1949, 71, 1095.

25. Johnson and Goldman, J.A.C.S., 1945, 68, 430.

26. Cronyn and Goodrich, J.A.C.S., 1952, 74, 3331.

27. Trippet, Advances in Organic Chemistry, Interscience Publishers Inc., New York, 1960, Vol. I, p. 83.

28. Campbell and Campbell, Chem. Revs. 1942, 31, 77.

29. Burwell, Chem. Revs. 1957, 52, 895.

30. Weidlich and Meyer-Delius, Ber. 1941, 74, 1195.

31. Dreiding and Tomasewski, J.A.C.S., 1954, 76, 540.

32. Bachmann and Morin, J.A.C.S., 1944, 66, 553.

33. Bachmann and Johnson, J.A.C.S., 1949, 71, 3463.

34. Kidd, Ph.D., thesis Edinburgh, 1954, p. 52.

35. Bachmann, J.A.C.S., 1940, 62, 824.

36. Anderson and Bell, J.C.S., 1961, 4705.

37. Hann and Lapworth, Proc. Chem. Soc. 1903, 19, 189.

Acknowledgements

I wish to express my sincere thanks to Dr. Neil Campbell, O.B.E., for the guidance and encouragement that he has given me during the course of this research work.

I am grateful to the Department of Scientific and Industrial Research for a maintenance allowance and to Professor E. L. Hirst, C.B.E., F.R.S., for the provision of laboratory facilities.

I am specially indebted to my wife Helen who typed this thesis.